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OF THE

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS

VOLUME XLI

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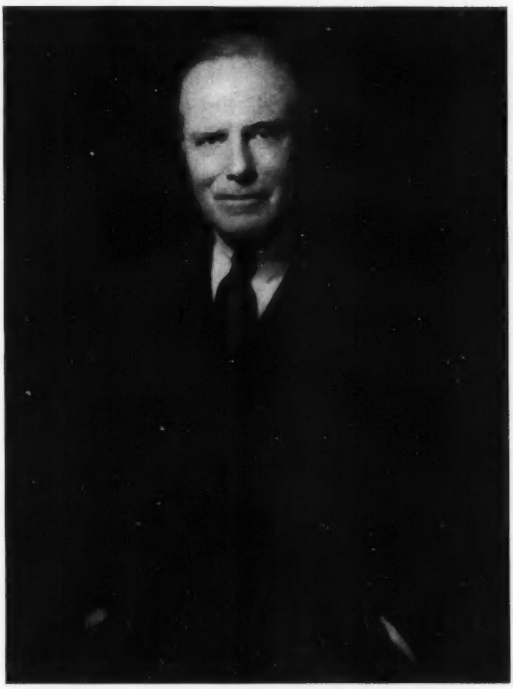
EDWARD L. KEYES, M.D.

1873–1949

Dr. Edward L. Keyes, aged 75, one of our most eminent and best beloved members, died at his home in New York on Wednesday, March 16, 1949, of an acute heart attack. Throughout his long life there was no endeavor to which he did not aspire and there were no high positions in the world of urology which he did not attain.



EDWARD L. KEYES, M.D.

Following in the footsteps of a distinguished father, he became equally eminent in the field of urology.

After obtaining his academic degree at Georgetown College, he received his medical degree from the College of Physicians and Surgeons, and interned in surgery at the New York Hospital.

He was professor of urology at Cornell Medical College for 23 years, director of urology for 12 years at Bellevue Hospital, and 13 years at St. Vincent's Hospital.

He was president, at various times, of the International Urological Society, the American Social Hygiene Association, the American Association of Genito-Urinary Surgeons, the American Urological Association and the Neisserian Society (honorary). He was vice-president of the New York Academy of Medicine and a member of many foreign urological societies. He was an honorary fellow in the Royal College of Surgeons, England, and was decorated as an officer of the French Legion of Honor.

During World War I, he rose to colonelcy as urologist to the Advance Section, American Expeditionary Forces.

He received the first award of the William Freeman Snow Medal for distinguished service in the field of social hygiene and was also the first recipient of the Keyes Medal of the American Association of Genito-Urinary Surgeons.

He contributed to medical journals, but his most notable writing was contained in several editions of *Urology*, a text-book.

No one of us can forget his ready wit, his charm, his innate sense of humor, his broad vision; we will miss him.

Surviving are his second wife, the former Mrs. Bessie Potter Vonnoh, sculptor, whom he married last June; two sons and two daughters by his first wife, the late Emma Willard Scudder Keyes.

This Association goes on record as expressing its deep sorrow at the passing of its beloved member. Be it resolved that this expression be spread on the minutes of this meeting and a copy be forwarded to members of his family.

ARCHIE L. DEAN

WILLIAM E. LOWER, M.D.

1867–1948

On June 17, 1948 the urological profession suffered the loss by death of one of its most prominent members, Dr. William Edgar Lower. Born May 6, 1867 in Canton, Ohio, the son of Henry and Mary Lower, Dr. Lower was graduated from the Western Reserve University Medical Department in 1891 and began his long practice in Cleveland the following year.

In 1896 when Lutheran Hospital was founded, he became a member of its first surgical staff, and for 24 years was its chief of staff. He had remained an attending surgeon there, and in 1946 completed his fiftieth year of association with the hospital.

Dr. Lower was also associate surgeon at Lakeside Hospital from 1910 to 1931, director of surgery at Mt. Sinai Hospital from 1919 to 1924, and associate professor of genito-urinary surgery at Western Reserve University from 1910 to 1931.

In 1900, during the Philippine insurrection, he served in the U. S. Army there as an assistant surgeon. During World War I he first served in the U. S. Army as a major and assistant surgical director of the Lakeside Base Hospital Unit in service with the British Expeditionary Force in France. In May 1918 he was promoted to lieutenant colonel and made the Unit's commanding officer.

On February 5, 1921 Dr. Lower, with Drs. George W. Crile, Frank E. Bunts, and John Phillips founded the Cleveland Clinic Foundation which opened the Clinic February 26 of the same year. He contributed much to Cleveland medicine, was an active member of the Academy of Medicine and served as its president in 1909. In 1938 the Academy made him an honorary member and in 1945 bestowed upon him its Distinguished Service Award for outstanding service to the community and to organized medicine.

He was a member and had served as president of the American Urological Association, American Association of Genito-Urinary Surgeons, Ohio State Medical Society, Cleveland Academy of Medicine, and the Interurban Surgical Society. He organized the Clinical Society of Genito-Urinary Surgeons, and was its first host and president.

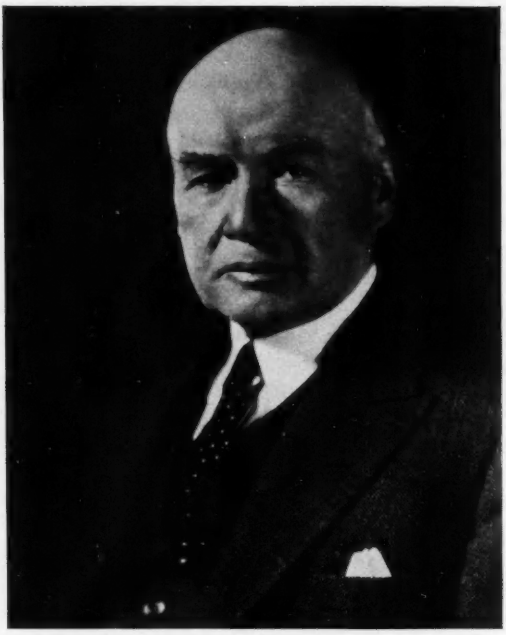
He was also a member of the American Surgical Association, the Society of Clinical Surgery, Société Internationale de Urologie, a fellow of the American Medical Association, American College of Surgeons, and the Southern Surgical Association.

Such factual data, however, do not quite portray him as an individual. To use the common vernacular, Dr. Lower "came up the hard way." He was from humble but sturdy pioneer stock and his boyhood was spent on the land. No doubt it was here that he learned his outstanding characteristics of hard work, thrift, frugality, and a restless urge to build better. Hard work and devotion to duty were part of his religion and he looked for this in others. Illustrative of this,

he always felt that it was bad training to start the New Year off with an idle holiday and on many occasions he scheduled regular operations on January first. If there were no operations, the house staff was called at the usual early hour for ward rounds.

He had a courageous but kindly heart which made him both feared and loved. He was no tyrant, but an exacting leader who expected no more than he gave. He could call down an errant subordinate with unforgettable vigor, yet listen patiently and give kindly advice to one who was in trouble.

In the consulting room he had a warmth of manner and quiet assurance that immediately commanded respect and confidence. For him the patients never



WILLIAM E. LOWER, M.D.

lost their identity and his medical opinions and advice always took into consideration the human aspects of the problem. The patient never became a number or an operation, even when the pressure of a busy practice might have excused this. When house officers reported cases he objected vigorously to referring to the patient as a male or female, preferring the term lady or gentleman as being more appropriate.

As a surgeon he was recognized for his judgment, skill, dexterity, and gentleness. This may best be summed up by saying that he made hard operations look easy. He insisted upon neatness as an indication of a good operation and his constant admonition to his assistants was "gently." He often said that you can

write a patient's convalescent record at the close of an operation and the usually uneventful postoperative course his patients followed was a glowing tribute to operations properly advised and skillfully and gently executed. He was a surgeon's surgeon.

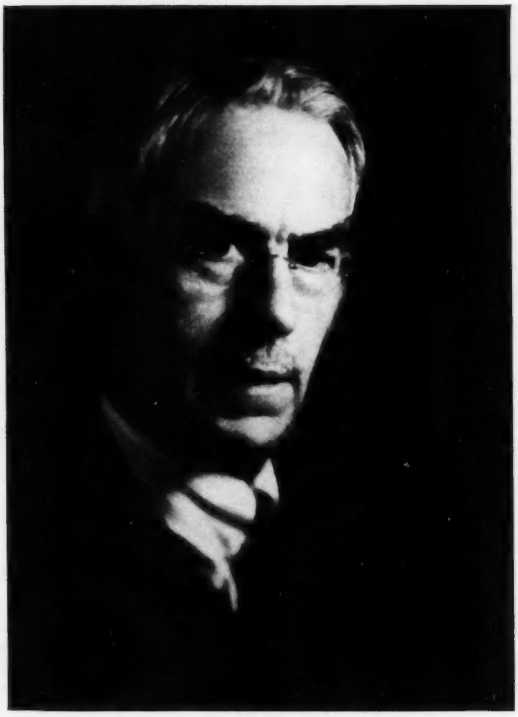
His many contributions to medicine and to urology need hardly be detailed to his friends in the profession. To those who did not know him so well let us say that he handed down the torch of honesty in practice, courage and dexterity in surgery, and unselfish devotion to medicine.

WILLIAM J. ENGEL

NATHANIEL P. RATHBUN, M.D.

1876–1949

Dr. Nathaniel Philip Rathbun died at The Brooklyn Hospital on February 26, 1949, after a long illness. He was born at Springfield, Massachusetts, August 17, 1876. He was graduated from the Stockbridge High School in 1893, and began the study of medicine under the old preceptorship system by serving as apprentice to a local physician in Stockbridge. He pursued his studies further at the Long



NATHANIEL P. RATHBUN, M.D.

Island College Hospital, receiving his doctor's degree in 1898. His selection as valedictorian of his class presaged the leadership he was to evidence throughout his entire professional career.

An internship at the Brooklyn Hospital, begun in 1898, was followed by a succession of appointments to positions on the staff. In 1913, he became a clinical assistant surgeon; in 1918, an associate surgeon and, in 1920, attending urologist.

It may truly be said that he established the urological service of the hospital, serving as its chief until January 1946.

The story of Doctor Rathbun's role of leadership in the field of Urology includes the founding of the Brooklyn Urological Society whose first meetings were held in his office. He served as president of that organization, and was later president of the New York Urological Society. He was also secretary of the Section on Urology of the New York Academy of Medicine 1922–23 and chairman in 1923–24. In recent years, he became a trustee of the Long Island College of Medicine. In 1934 also, he became a founding member of the American Board of Urology, serving on that Board until his resignation in 1947. He was also a member of the International Urological Association, the American Medical Association, the Brooklyn Surgical Society, of which he was an honorary member, and the American College of Surgeons.

Dr. Rathbun was elected to membership in the American Association of Genito-Urinary Surgeons in 1921. He prized his membership in this organization highly and was one of its most loyal and enthusiastic members. He thoroughly enjoyed attending the annual meetings where he could enjoy seeing his many friends. He served as president in 1943.

At the time of his death, he held consulting appointments to The Brooklyn, Lutheran, Norwegian Lutheran Deaconesses', Beth El, Bushwick and the Eastern Long Island (Greenport) Hospitals. Doctor Rathbun contributed many valuable papers to urological literature. In spite of his numerous interests within the field of his chosen specialty, he found time for extensive reading of good literature, for golf, and for varied social activities. His sincerity, his constant endeavors in the interest of the American Association of Genito-Urinary Surgeons and his charming personal qualities deeply endeared him to the members of this Association.

Therefore, be it resolved that the members of the American Association of Genito-Urinary Surgeons express their profound grief at the loss of so distinguished and beloved a contemporary by recording these resolutions in the minutes of this society and by sending copies of them to the members of Doctor Rathbun's family, with deepest sympathy.

FRANK C. HAMM

STONE IN THE URETERAL STUMP LEFT WHEN NEPHRECTOMY IS DONE

GEORGE R. LIVERMORE

Sometimes, due to the condition of the patient, certain complications, or late pregnancy, it is not possible or it is deemed unwise to remove a stone from the ureter at the time a nephrectomy is done. Ljunggren (1948) reported a case of infected ureteral stump removed 18 years after nephrectomy and cited cases reported by Enderlein, Rodelius, Lower, Haslinger and Kidd and 2 other cases, previously reported, of his own. It is said that stone non-infected or those with low grade infection usually cause no trouble when left in the ureteral stump following nephrectomy. This is true in the majority of cases, as concurred in by Scholl, Bumpus, and McMahon.

However, when the ureter is dilated, thus leaving an infected pouch that communicates with the bladder, and in that type in which the ureter retains its peristaltic action, mucopurulent material is carried or injected into the bladder. This results in a persistent cystitis and probable pyelonephritis unless this source of infection is removed. When the infected material is retained in the ureteral stump peri-ureteral abscess may occur as in my third case herewith reported.

Cases have also been reported in which stones have formed in the ureteral stump after nephrectomy. Ojetti says that stone formation in the nephrectomized ureter is extremely rare and that most reported cases were intentionally left at the time of nephrectomy. It is a fact, too, that those reported to have formed after nephrectomy may have been overlooked when the kidney was removed.

Ojetti reports a case of his own, a man aged 53, whose left kidney had been removed 15 years before he came under his care. At intervals since the nephrectomy he had suffered from attacks of pain in his left iliac region and at times fever and cloudy urine. On admission to the hospital his urine was normal but there was tenderness over the midportion of the left ureter. X-ray showed three shadows in the lower portion of the left ureter. At operation the ureteral stump was completely excised and when opened contained purulent urine and three calculi. He believed the stones had been present at the time the nephrectomy had been done. He councils care in calculosis to prevent stones in the kidney from being forced down the ureter and left when the kidney is removed. The author concurs in the above as he has had the experience of stones moving from the kidney pelvis down the ureter and those in the ureter passing upward into the pelvis. Fortunately, such mishaps were noted at the time of operation and the runaway stones found and removed, though sometimes at the expense of a second incision.

Ojetti says true recurrences of stones in the ureteral stump remain hypothetical. I personally have not seen such a case.

Bumpus cites 3 cases in which a stone left in the ureter at the time nephrectomy was done caused complications that necessitated removal of the ureteral stump

in two of them. In 1 case the secondary operation was performed 1 year after nephrectomy and in the other, 2 years.

McMahon cites one 20 years after nephrectomy, the patient having had no symptoms until 19 years after her operation when she developed left lower ureteral colic which radiated to the left labium. She had a second attack a few months later and a third a few days before admission to the hospital. Frequency, burning and hematuria were present with the third attack of colic. This patient, in addition to the stone in the ureter, had a papilloma of the bladder in the left ureteral orifice.

I have seen 3 cases in which a stone left in the ureteral stump when nephrectomy was done caused so much suffering and morbidity that operation for removal of the stone became necessary.

The first case was that of a man 22 years of age who had right hydronephrosis due to a large stone in his right ureter. The nephrectomy was difficult and hemorrhage profuse. The urologist who performed it deemed it unwise to attempt to remove the ureteral stone. This patient had no symptoms for a year, then he began suffering frequency, burning and low grade fever. I saw him at this time; on cystoscopy, pus could be seen exuding from the right ureteral orifice. Irrigations of the ureteral stump with mercurochrome 2 per cent and later silver nitrate 1 per cent resulted in only temporary improvement. I, therefore, operated and removed the stone with prompt and permanent relief.

The second case was that of a man 40 years of age who had left pyonephrosis, the result of blockage of the left ureter by a large stone. I did a left nephrectomy which was quite difficult. The patient went into shock and hence the removal of the ureteral stone was not done. He continued to have frequency, burning, chills and fever, despite irrigations of the ureteral stump. Therefore, I removed the stone and the patient made a prompt recovery. The ureteral stump, however, was irrigated two or three times at weekly intervals before all infection cleared up.

The third case I shall report in detail.

L. H. S., a white man, married, aged 50, was first seen June 28, 1939. He had had rigors, fever, sweats and pus in the urine off and on since March 1938. Urologic study showed a stone 4 cm. long by 3 cm. wide in the right kidney pelvis; also a stone $3\frac{1}{2}$ cm. by $2\frac{1}{2}$ cm. in the upper third of his right ureter. Thick yellow pus could be seen oozing from the right ureteral orifice. Nothing could be passed beyond the ureteral stone. His blood pressure was 135/80.

The diagnosis was stone in lower third of right ureter too large to pass, and right calculous pyonephrosis.

On August 23, 1939 a right nephrectomy was done. Owing to difficulty in freeing the kidney, the peritoneum was torn and the patient went into shock. Hence, no attempt was made to remove the stone in the right ureter which, at this time, was in the upper third. He made a nice recovery and left the hospital on the fourteenth day.

He was not seen again until October 16, 1939, about one and three-fourth months after the nephrectomy. He was in fine condition, had gained 5 pounds

and said he felt like a new man. However, a urinalysis showed 10 pus cells to the high power field. He refused cystoscopic treatment. He was not seen again until March 18, 1940 when he returned with left renal colic. On cystoscopy and the passage of a catheter to his left kidney pelvis 120 cc clear retention urine was obtained. A pyelogram was unsatisfactory. The stone in the right ureteral stump had now passed downward below the crest of the ileum and a small shadow could be seen in the lower portion of his left ureter. No pus could be seen exuding from the right ureteral orifice.

May 5, 1940, he had severe left ureteral colic and later passed a small calculus which was chiefly calcium phosphate. He was put on an acid ash diet. He was not seen again until February 11, 1944 when he stated he had been in quite good

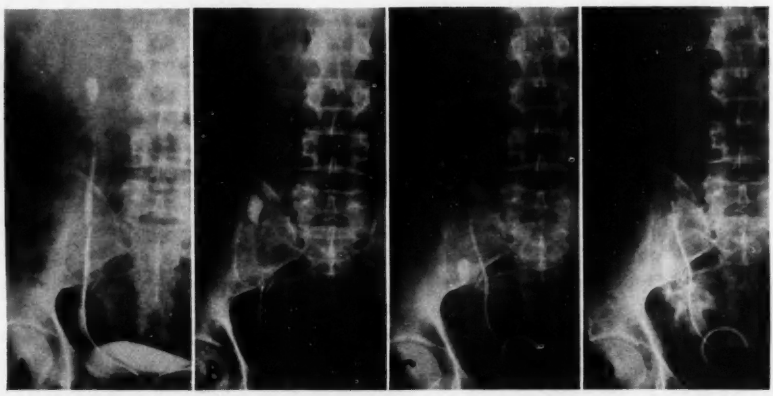


FIG. 1. *A*, June 28, 1949. Stone in upper third of stump of right ureter. *B*, May 5, 1940. Stone in stump of right ureter below crest of ileum. *C*, December 5, 1947. Stone in stump of right ureter at pelvic brim. *D*, December 5, 1947. Stone shown with extravasation of medium into abscess cavity about ureter and stone.

health. Urinalysis showed 5 pus cells to the high power field. X-ray showed a stone in the right ureteral stump as before. On cystoscopy no pus was seen coming from the right ureteral orifice and clear urine from left, that showed only a rare pus cell and cultures were negative.

He was not seen again until October 1947 when conditions were the same as on last examination except that he had pain in his right inguinal region. On cystoscopy, pus could be seen exuding from right ureteral orifice. The stone was in the right ureteral stump as before. Removal of the stone from the ureter was advised but the patient refused.

He was not seen again until December 5, 1947, when he returned with history of dull aching pain in right lower quadrant, rigors, fever and sweats at intervals of 3 days to 2 weeks, beginning about 1 month ago. He had had 5 injections of penicillin 300,000 units each. This had controlled the rigors and fever, but pain and soreness in the right inguinal region had persisted. Cystoscopy and x-ray showed pus exuding from the right ureteral orifice. Clear urine came from the left side and the function of the left kidney was good. Indigo carmine appeared

in 2 minutes, deep in 2½ minutes. X-ray showed that the stone in the right ureteral stump had fallen to the pelvic brim and looked as though the ureter had bent downward on itself. There was extravasation of the pyelographic medium outside the ureter and irregularly about the stone. There was marked induration above and to the right of the symphysis.

The diagnosis was stone in the ureteral stump, abscess with rupture of ureter and extravasation of pus about the stone and ureter.

Operation on December 11, 1947 disclosed a large abscess about the ureteral stump at the site of the stone. I was able to remove the stone and evacuate about 2 ounces of yellow pus, but the ureter was so densely adherent that it could not be freed. Sulfanilamide crystals were dusted in, and the abscess cavity packed with gauze and a cigarette drain; the wound was closed to the gauze drainage by means of silkworm and chromic gut sutures. The patient made a nice recovery and left the hospital on the twelfth postoperative day.

January 2, 1948, he returned to the office with wound completely healed and feeling perfectly well. Urinalysis showed only an occasional pus cell. The red cell count was 4,850,000.

CONCLUSIONS

A calculus left in the ureter at the time nephrectomy is done is a potential source of danger.

If pus exudes into the bladder from the ureteral stump and the infection cannot be cleared up by ureteral lavage and medication appropriate for the type of organism, operation should not be delayed.

Persistent cystitis or peri-ureteral abscess demands operation at once.

Three personal cases and others from the literature are herewith reported.

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URINARY UREASE, CRYSTALLURIA AND RECURRENT STONE FORMATION: PRELIMINARY REPORT

EMERSON SMITH AND (by invitation) JOHN F. McINTOSH

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The relation of urea-splitting organisms to disease of the urinary tract was first studied as a bacteriological problem. Hager and Magath led the way in 1925–26, when they described Proteus ammoniae as the cause of alkaline encrusted cystitis. Laidley's paper in 1930 made an extensive survey of urease production by organisms isolated from the urinary tract. From his studies and those of others it is evident that a considerable number of bacterial species are capable of splitting urea. A review of the literature leaves one with the impression that the use of artificial media cannot fail to introduce an arbitrary factor into the bacteriological findings. This is probably one of the reasons that correlation between bacteriological tests for urease-producing organisms and other laboratory data sometimes leaves something to be desired. This poor correlation with clinical conditions has been discussed by Thompson and Schulte (1939).

In spite of difficulties of method and of interpretation, the surgical implications of these discoveries have not been neglected by urologists. Important contributions are those of Brown and Earlam (1933), Fowler (1934), Hellström (1936, 1938) Twinem (1937), and of Chute and Suby (1940). Some of these authors, especially Hellström, Fowler, and Twinem, have laid special emphasis upon the importance of staphylococcal infection of the kidney in relation to the formation and recurrence of stone. With this view we are not in agreement, and we shall have occasion to return to the relative importance of the Staphylococcus at a later point. For the moment we will only note that a high degree of correlation between urinary infection with urea-splitting organisms and the formation of recurrent phosphatic calculi may be regarded as firmly established.

Closely related to these cases of postoperative recurrence and likewise associated with infection by urea-splitting organisms are the habitual stone-formers who are able to pass the concretions by the natural channels. These cases merge with a third group which tend to pass crystalline and amorphous phosphates, and which, for lack of a better name, may be called cases of crystalluria. All these cases are characterized by infection which is shown by the presence of pus in the urine, and by urea-splitting organisms which may be found on culture. They are to be distinguished from cases of essential phosphaturia in which pus is absent, and in which the urine is sterile on culture.

In our opinion, then, there are two types of phosphaturia which require to be distinguished from one another. One type has infected alkaline urine, the other sterile urine which may be neutral or alkaline. It is the infected type of phosphaturia with which we are concerned. In the urine sediment of such a case two sorts of phosphate deposit are likely to be found. One of these contains calcium and is

commonly spoken of as amorphous phosphate. The other is a crystalline deposit containing ammonium and magnesium, and is ordinarily referred to as triple phosphate. It is now usual to refer to these substances as apatite and struvite respectively.

In theory all of this is simple enough, and may be found in any textbook. In practice, we have been impressed with the difficulties which stand in the way of a precise diagnosis of cases of this kind. A patient may have symptoms of calculus with characteristic findings in the x-rays, and on microscopic examination of the urine. But several cultures of the urine may be necessary before it is possible to say whether a urea-splitting organism is likely to be responsible for the disease. We have recently reviewed our own experience with urine culture in stone cases. The striking thing about these routine cultures is their inconsistency. We believe that a large proportion of the organisms found have no clinical significance, and that external contaminants are all too frequent. We have reason to think that other urologists have had similar experience.

It therefore occurred to us that as a supplement to the usual bacteriologic studies we should try to measure the urease associated with the urea-splitting organisms in the urine by biochemical methods.[1] Such a test, if positive, would make it possible to diagnose the presence of disease caused by urea-splitting organisms quickly and easily. As far as we are aware, quantitative tests of this sort have not been made previously.

After some experimenting, we have found that determinable amounts of urease are present in the urine sediment in certain cases, and that it is possible to measure the enzyme quantitatively. We have made use of a modification of Van Slyke and Archibald's (1944) colorimetric timing method. The urease acts on urea in a phosphate buffer solution and one observes how long it takes the *p*H to rise to a definite point. In our tests we have used a photocell colorimeter to follow the reaction, and to determine the end-point. The amount of enzyme present is inversely proportional to the length of time it takes for the *p*H to rise from 6.7 to 7.7. The amount of urease is expressed in Sumner units. This unit is the amount of urease capable of producing 1 mg. of ammonia nitrogen in 5 minutes at 20 degrees centigrade, under specific conditions.

We have been using the test for about a year and a half. When there is heavy

[1] *Test for the amount of urease in urine sediment:*
(1) Buffered urea solution (*p*H 6.7)
1 cc 1 Molar NaH_2PO_4
1 cc 1 Molar K_2HPO_4
3 gm. urea
5 cc phenol red indicator (B.D.H.)
Distilled water to make 100 cc
(2) Control buffer of *p*H 7.7
Into a 100 cc graduated cylinder measure 1 cc of Molar NaH_2PO_4, 7 cc of Molar K_2HPO_4, and 4 cc of phenol red indicator. Dilute to 80 cc.
Procedure: A fresh specimen of urine is thoroughly mixed. A suitable amount (usually 15 to 60 cc) is centrifuged, and the supernatant discarded. The sediment, usually in 0.5 cc volume, is transferred to the absorption cell of a colorimeter, and 5 cc of the buffered urea solution is added. A galvanometer reading is taken at once, using a suitable green filter, several readings are taken at intervals until the end point is reached.
The end point is determined by finding the difference in opacity between the buffered urea solution and the control buffer of *p*H 7.7.

infection with a urea-splitting organism, such as in alkaline encrusted cystitis, high values are found, of the order of 50 Sumner units per liter. In these cases the tests may be completed in 10 or 15 minutes. A case with a phosphatic staghorn calculus might show one Sumner unit per liter. When there is little infection, or when the urea-splitting power of the organism is slight, the amount of urease may be so slight as to present difficulty in measurement. It is still too early to form an opinion about its limitations. A few typical results are summarized in table 1.

We have used the test before and after treatment in a series of 6 cases characterized by recurrent stone formation and crystalluria. It has seemed to us that these cases may serve to illustrate the relation between stone formation and the urea-splitting enzyme in a useful way. The following are two typical examples.

TABLE 1

CASE NO.	DIAGNOSIS	URINE CULTURE	URINARY UREASE	
			units per liter	
1	Encrusted cystitis	Proteus vulgaris	64.	16.5
2	Encrusted cystitis	P. morganii, A. aerogenes	40.	14.5
3	Prostatism, postoperative	P. mirabilis	51.	
4	Staghorn calculus, bilat.	Micrococcus	1.7	0.4
5	Staghorn calculus, bilat.	Micrococcus	0.6	
6	Renal calculus, bilat.	Micrococcus	0.4	
7	Renal calculus, cystinuria	Pseudomonas aeruginosa	0.05	
8	Renal calculus, bilat.	P. aeruginosa	0.0	
9	Cord bladder, cystitis	E. coli, A. aerogenes	0.0	
10	Renal calculus	E. coli	0.0	

CASE REPORTS

Case 1 (fig. 1). A man aged 49 years had passed "gritty urine" for many years. The left kidney was found to contain a staghorn phosphatic calculus, and was removed. After operation the urine continued to be alkaline, loaded with crystals, and positive for urease. Micrococcus was isolated from it on four occasions. He was then given a course of intramuscular injections of penicillin for 5 days. On the day following the first dose the struvite crystals disappeared from the urine and have never re-appeared. The urease content fell from four units to zero. The urine changed from alkaline to acid in reaction, and there was a marked diminution in the amount of pus present. At the end of 4 months these normal findings are still present. The patient has experienced marked relief of dyspepsia which has troubled him for years.

Case 2 (fig. 2). A man aged 49 years complained of burning on micturition and passage of sand and calculi. Pyelotomies had been done for stones in 1925 and 1926, and nephrectomy for the same reason in 1936. From 1937 to 1948 he had been troubled by the passage of sand on many occasions and sometimes passage of stones. On culture of the urine a urea-splitting Micrococcus, highly sensitive to penicillin, was recovered on two occasions. The urease content of

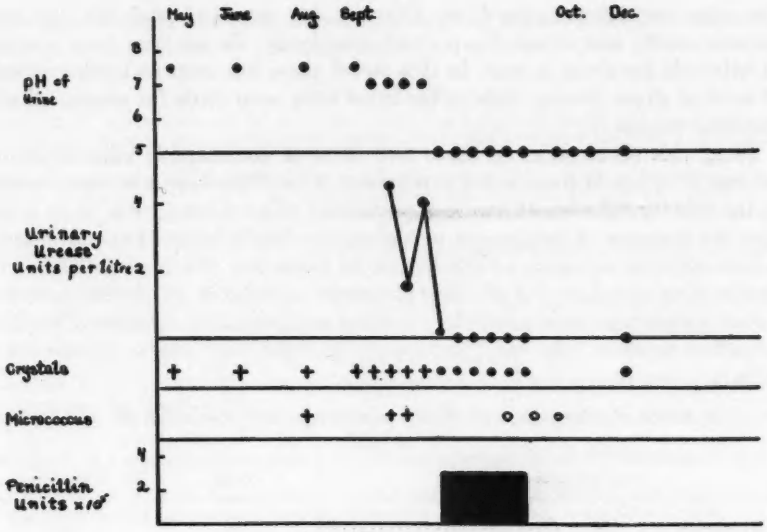
May
June
Aug.
Sept.
Oct.
Dec.
pH of Urine
8
7
6
5
4
Urinary Urease Units per litre
2
Crystals
Micrococcus
4
Penicillin Units x10⁵
2

FIG. 1.

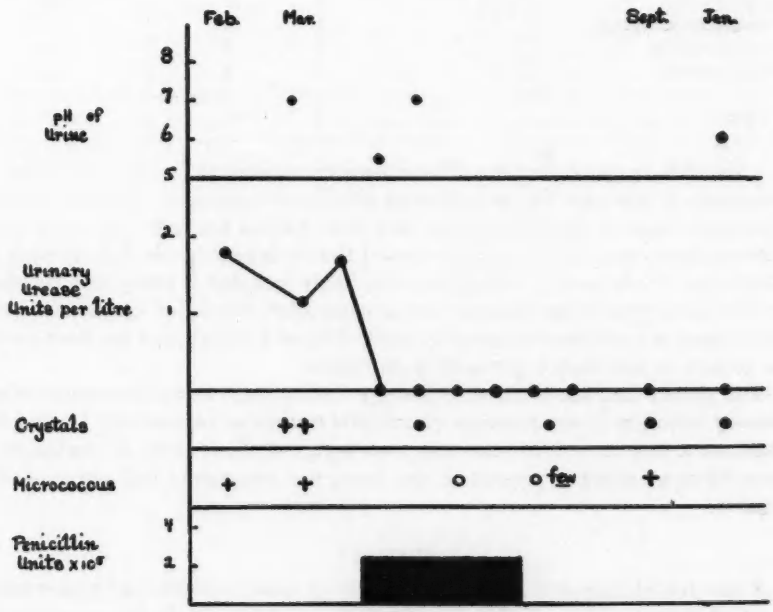
Feb.
Mar.
Sept.
Jan.
pH of Urine
8
7
6
5
2
Urinary Urease Units per litre
1
Crystals
Micrococcus
few
4
Penicillin Units x10⁵
2

FIG. 2.

the urine was 1.8 units per liter. After a 4 day course of penicillin, the urine became sterile, and urease disappeared completely. He has now been observed at intervals for about a year. In this period there has been no further passage of sand or stone. Several tests of the urine have been made for urease, all with negative results.

From this short series of cases two facts of considerable clinical interest emerge. The first of these is the importance of the Micrococcus in the formation of the urinary calculus. It has been previously pointed out by one of us (1942) that the presence of magnesium in a stone is a useful index of the presence of a urea-splitting organism at the site of its formation. We have tabulated the results of urine cultures in 93 cases of urinary calculus in which the stone contained struvite, as determined by chemical analysis. This tabulation has been simplified to show only the "predominating organism," and is reproduced in table 2.

TABLE 2. *Result of urine culture in 93 cases of urinary calculus in which the stone contained struvite*

PREDOMINATING ORGANISM	CASES	PER CENT
Micrococcus	35	37.6
Proteus	22	23.6
E. coli	11	11.8
Pseudomonas	11	11.8
Aerobacter aerogenes	5	5.4
Staphylococcus	5	5.4
Streptococcus	4	4.3
Total	93	99.9

This table suggests that the Micrococcus is responsible for over one third of the stones of this type. In our judgment this figure is probably too conservative. The importance of the Micrococcus as a stone-former has been lost sight of by some authors, some of whom have denied that it is pathogenic. Others such as Hellström, Fowler, and Twinem, have probably included it along with its close relative, Staphylococcus pyogenes. In our experience, Staphylococcus is relatively uncommon as a producer of urease in cases of urinary calculi, and has been found on culture in less than 5 per cent of our cases.

The second fact has to do with therapy. It has been well substantiated that urinary infection in the presence of calculus cannot be successfully treated by antibiotics. Our experience indicates that many of these cases, if treated at a time when no stone is present in the tract, are completely and permanently curable.

SUMMARY

A new test is suggested for use in the study of cases in which the urinary tract is infected by an urea-splitting organism. This test consists in the quantitative determination of the urease present in the sediment of the fresh urine.

The importance of the Micrococcus as a cause of urinary infection and stone formation is emphasized by our experience.

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PARATHYROID ADENOMA AND RENAL CALCULI

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Every urologist who is interested in the relationship of parathyroid disease to renal calculi should read "A Page Out of the History of Hyperparathyroidism" by Fuller Albright. Here he will find an excellent review of the development of our knowledge of the parathyroid glands. Also presented in great detail is the important role played by Erdheim in the development of our knowledge of the relationship between the parathyroid glands and calcium metabolism. It is gratifying to have Albright emphasize the value of Erdheim's contributions to our knowledge of this subject, since it has not received the recognition it deserves.

It was my privilege to work with Erdheim when he made his epoch making observations on the disturbances of the physiology of the parathyroids. He told me he became interested at the suggestion of Professor Dr. Anton Freiherr Von Eiselsberg who had operated upon a patient with a goitre. Following the operation the patient developed tetany and Eiselsberg wanted Erdheim to tell him why the patient developed tetany.

It is to be remembered that Erdheim made his first observations in 1906, long before the birth of modern endocrinology.

The relationship between lesions of the parathyroids and renal calculi was first called to our attention by Fuller Albright and his co-workers in Boston.

Because of the increasing interest in the subject of the relationship between lesions of the parathyroid glands and renal calculi, I would like to present the following 4 cases. Although the association of parathyroid disease and renal calculi is not very common and will be discussed further in the paper, I would at this point like to emphasize the fact that in cases showing a history of recurrent stones, or a history of many operations for stones, the possibility of the cause for these recurrences should be sought for in the parathyroid glands.

CASE REPORTS

Case 1. Mrs. V. B., aged 35, referred by Dr. M. F. Russell of Great Bend, Kansas, was admitted to Presbyterian Hospital on November 4, 1948. In 1941 following an attack of the "flu" she developed severe colicky pain in the left side of the abdomen, which terminated with the passage of a stone. The patient stated that during the past 7 years she had had 75 cystoscopic examinations and 300 x-ray examinations. In August 1946, within a period of 10 days, she underwent 3 operations for kidney and ureteral stones. After her operations she had more than 20 attacks of renal colic. In about one-half of these attacks the patient subsequently passed calculi. During some of the attacks she had dysuria and hematuria. Her present attack began one week before admission to the Pres-

byterian Hospital. She had severe attacks of pain associated with nausea, vomiting, and belching of gas. She was obliged to void from 30 to 40 times a day and from 12 to 14 times a night. There was some stiffness in the hips, knees and shoulders. For 10 days before admission she had substernal pain associated with the taking of food. There was no history of muscular twitching, spasms, or convulsions.

The temperature was 98.6 F, respiratory rate 16/minute, pulse rate 132/minute. Blood pressure 100/70. A palpable mass was found over the right lobe of the thyroid gland. A diagnosis of enlargement of the parathyroid was made. The heart was slightly enlarged. A harsh, short presystolic murmur was heard over the precordium. The abdomen showed four surgical scars: right lumbar, one at border of right rectus, one in the midline, and one at border of left rectus. There was pain and tenderness extending laterally on either side of the umbilicus. The lower pole of the right kidney was palpable. The extremities were normal.

Urinalysis: Reaction alkaline, specific gravity 1.013, albumin 1+; sugar 0; slight trace of blood; sediment showed many bacteria and phosphate crystals. Blood: Kahn test negative; hemoglobin 13.5 gm.; red blood cells 4,500,000; white blood cells 8,000. Blood chemistry: Nonprotein nitrogen 44 mg. per cent; calcium 16.3 mg. per cent; phosphorus 2.6 mg. per cent.

X-rays showed two stone shadows over the right kidney pelvis, multiple stone shadows over the lower pole of the left kidney, and one large shadow along course of right ureter.

Cystoscopic examination November 8, 1948 showed that the bladder was normal. The ureteral catheter met an obstruction in the left lower ureter at a point corresponding with the location of the stone.

The tentative diagnosis was parathyroid adenoma and renal calculi.

Eleven hours after the cystoscopic examination there was marked lassitude, great fatigue, and pain in both knees.

On November 9, the day following the cystoscopic examination, the patient went into profound shock. She was given two transfusions of 500 cc of whole blood and 500 cc of plasma. The blood pressure was systolic 80, diastolic 68.

On November 10 the patient was seen in consultation with Dr. Earl Gray, who advised adrenal cortical extract. It was given with no apparent result.

On November 11, the temperature was 102 F. The nonprotein nitrogen was 80 mg. per cent and the blood pressure was 90.

On November 12 at noon the blood pressure was 78/70. When blood pressure cuff was inflated, the patient developed tetanic contractions in the arm. The temperature was 103 F rectally. The patient died 2 hours later.

The sequence of events following the cystoscopic examination were interpreted as due to a parathyroid crisis.

The autopsy report by Dr. George Hass is as follows: 1) adenoma of parathyroid gland; 2) hyperparathyroidism; 3) bilateral renal calculi; 4) ureteral calculus, left; 5) acute and chronic bilateral pyelonephritis; 6) hydronephrosis, left; 7) meningeal hemorrhage of undetermined origin (subarachnoid hemorrhage); 8) passive congestion of liver, spleen, and kidneys; 9) nabothian cysts; 10) acute

gastritis. There were two small stones in the calyces of the right kidney. There was a stone in one of the minor calyces of the left kidney and in the renal pelvis. There was a stone about 1 cm. in diameter impacted in the left lower ureter.

A firm nodule, 2 by 3 by 2.5 cm. was found in the lower pole of the right lobe of the thyroid. Microscopic examination showed parathyroid adenoma.

The bones and bone marrow were negative.

Summary: The patient had a parathyroid adenoma of at least 7 years' duration, as evidenced by the recurrent episodes of renal calculi. It is impossible to estimate how long the adenoma might have been present before the renal symptoms developed. There was no apparent evidence of skeletal abnormality in this case.

The possibility of an acute hyperparathyroid crisis was considered in this case, which will be discussed further in this paper.

Case 2. Mrs. N. T. N., aged 51, referred by Dr. H. L. Baker, was admitted to Presbyterian Hospital on July 22, 1945 and discharged on August 4, 1945. Three years previously the patient had a left nephrectomy (elsewhere) for renal calculi and a severe hydronephrosis. Six months ago severe pain developed in the right side which had been more or less constant. One week ago she had an extremely severe attack of renal colic, for which she was sent to the hospital.

Physical examination was negative.

Blood count: red cells 3,140,000; white cells 6,900; hemoglobin 11.2 gm. Urinalysis: albumin 3+; sugar 0; blood 3+; sediment showed many fresh red blood cells. Blood chemistry: calcium 12.5 mg. per cent; phosphorus, specimen lost; urea nitrogen 21 mg. per cent; nonprotein nitrogen 62 mg. per cent.

X-ray on July 20, 1945 showed a large stone in the right renal pelvis.

Cystoscopy on July 21, 1945 was negative.

Operation (H. L. K.): July 23, 1945, right pyelotomy, with removal of stone. An x-ray taken at the time that the kidney was exposed showed the kidney free of stone. Convalescence was uneventful and the patient left the hospital on August 4, 1945.

Chemical examination of the stone showed calcium oxalate, calcium phosphate, ammonium urate.

The patient was again admitted to the Presbyterian Hospital on December 1, 1946 on the service of Dr. H. L. Baker. She complained of polydypsia and frequency of urination both day and night for 3 months. There was marked fatigue and she tired easily. There was an ache in the left radius. Recently she had noted a mass in the neck in the right side.

Physical examination revealed a swelling in the neck on the right side which was interpreted as adenoma of the parathyroid gland.

X-rays showed an area of cystic bone destruction in the upper end of the left ulna and in the middle of the left second metatarsal bone of the foot. Both showed pathological fractures. Diagnosis: osteitis fibrosa cystica.

Blood count revealed erythrocytes 3.97 million; hemoglobin 12.0 gm.; leukocytes 7,400. Urinalysis: specific gravity 1.015; albumin 0; sugar 0; microscopic study showed only occasional erythrocytes and leukocytes. Blood chemistry:

December 2, 1946, calcium 12.1 mg. per cent; blood nonprotein nitrogen 39 mg. per cent; December 3, 1946, phosphorus 3.0 mg. per cent; alkaline phosphatase 50.0 units.

Operation (Dr. H. L. Baker): December 4, 1946, removal of parathyroid tumor. Microscopic diagnosis by Dr. George Hass: Adenoma of the parathyroid.

The patient made a smooth and uneventful convalescence and was discharged on December 14, 1946. Following the removal of the parathyroid adenoma there was a prompt drop in the blood calcium as well as in the nonprotein nitrogen. December 6, 1946, calcium 9.6 mg. per cent, blood nonprotein nitrogen 46 mg. per cent. December 10, 1946, calcium 7.6 mg. per cent; blood nonprotein nitrogen 33 mg. per cent.

Comment: From this history and the sequence of events, are we justified to assume that the patient had a parathyroid disease at the time of her first nephrectomy for stone?

Case 3. Mrs. G. W., aged 33, was admitted to Presbyterian Hospital on January 6, 1939. The patient had an attack of appendicitis 9 years ago; it subsided without operation. Two years ago she developed renal colic and a urinary stone was removed by operation elsewhere. On November 13, 1938, the patient was operated upon in the Presbyterian Hospital by Dr. V. C. David. Cholecystectomy for cholelithiasis was done. During her convalescence, the patient passed two small urinary calculi and after she left the hospital, she passed an additional calculus. On admission the complaint was severe pain in the right flank, associated with nausea and fever of 1 week's duration and a knowledge of kidney stones.

A circumscribed nodule, 1 cm. in diameter, was found in the right lower pole of the thyroid gland and a smaller nodule over the left lower pole of the thyroid gland. There was marked right costovertebral tenderness and rigidity of the right flank muscles. The blood pressure was 130/70, temperature 99.8 F, hemoglobin 85 per cent, red blood cells 4,500,000, white blood cells 13,400. Urinalysis: albumin 0, sugar 0; microscopic examination showed 50 red blood cells and 50 white blood cells per cu.m.m. Culture of the urine showed a growth of diplostreptococci in urine from left kidney. Urine from the right kidney was sterile. The Sulkowitch test was strongly positive. The phenolsulfonphthalein test showed an appearance time of 30 minutes, 5 per cent from the right kidney and 7 per cent from the left kidney. The nonprotein nitrogen was 46 mg. per cent.

January 9, 1939, serum calcium 17.3 mg. per cent
serum phosphorus 2 mg. per cent
January 16, 1939, serium calcium 17.9 mg. per cent
serum phosphorus 3 mg. per cent
January 17, 1939, serum calcium 18.1 mg. per cent
serum phosphorus 3.3 mg. per cent
January 26, 1939, serum calcium 20.8 mg. per cent
March 17, 1939 serum calcium 13.8 mg. per cent

X-ray examination of the genito-urinary tract showed a stone in the right

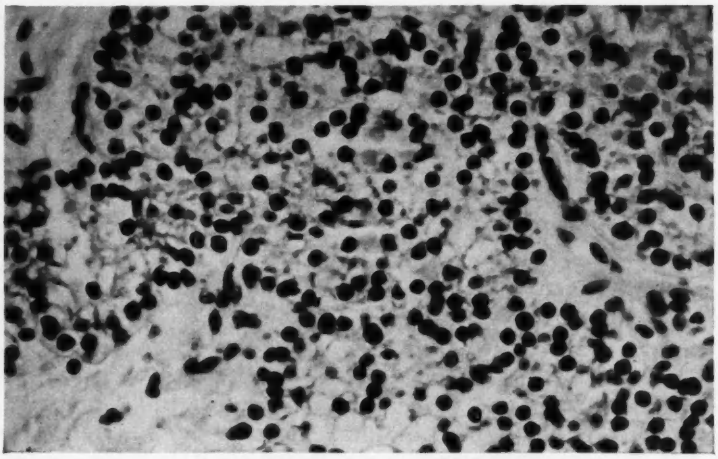

FIG. 1. Case 2. Parathyroid adenoma

FIG. 2. Case 2. Bone cyst with fracture of left ulna

ureter. X-rays of the chest were negative. Films of the skull, long bones, pelvis and ribs were normal.

Cystoscopic examination was negative.

The preoperative diagnosis was renal lithiasis due to a parathyroid adenoma.

Operation (H. L. K.): January 10, 1939, right ureterolithotomy. Following removal of the stone a large quantity of rich creamy pus drained from the ureteral incision. A soft rubber catheter was placed in the ureter through the incision.

Convalescence was uneventful except for occasional nausea and vomiting presumed to be on a basis of hyperparathyroidism, and an acute upper respiratory infection.

Chemical examination of stone revealed calcium carbonate, triple phosphates and calcium oxalates.

On April 6, 1939, Dr. Vernon David removed a parathyroid adenoma from the left lower lobe of the thyroid. Microscopic diagnosis: parathyroid adenoma.

Convalescence was uneventful and the patient was discharged on April 21, 1939 in excellent condition.

Case 4. Mr. E. F. T., aged 35, was admitted on December 27, 1947 on the service of Dr. N. J. Heckel, Presbyterian Hospital. In 1944 he had a right nephrectomy (elsewhere) for renal calculi and in 1946 he had a left ureterolithotomy for stone (elsewhere). In 1947 he passed a urinary stone. The patient also had a history of a duodenal ulcer. He had vomited blood. The patient was admitted to the hospital with severe renal colic on the left side. He had pain in the left costovertebral angle which radiated downward to the left flank but not to the abdomen. The patient had passed no urine for the previous 20 hours before he entered the hospital. This was due to a complete block of the ureter of his only kidney.

Temperature on admission was 100 F. Blood pressure 120/80. Pulse 120.

No palpable masses were detected in the neck. The heart and lungs were negative. The abdomen showed tenderness in the left flank.

X-rays showed a large stone in the upper ureteropelvic junction with stone shadows in the lower pole of the left kidney and in the region of the prostate. Intravenous urograms elsewhere 1 week before he came to the Presbyterian Hospital showed dilatation of the pelvis and calyces and upper ureter on the left side.

Hemoglobin 12.5 gm., red blood cells 3,850,000, white blood cells 20,000. Urine: acid, albumin +, sugar 0, casts 0, nonprotein nitrogen 60 mg. per cent.

Operation (H. L. K.); left pyelotomy and removal of a stone impacted in the ureteropelvic junction. Six smaller calculi were removed from the lower calyx. Several pieces of kidney showing small abscesses on the surface were removed. The pathological diagnosis was "calculi in the pelvis and abscesses in the cortex of the left kidney."

The chemical examination of the calculi revealed calcium phosphate and oxalate. Cultures at the time of operation revealed B. aerogenes and B. coli.

The patient was discharged on the fifteenth hospital day.

The second admission to Presbyterian Hospital was on May 17, 1948, on the service of Dr. Stanton Lawton. The patient complained of acute, generalized

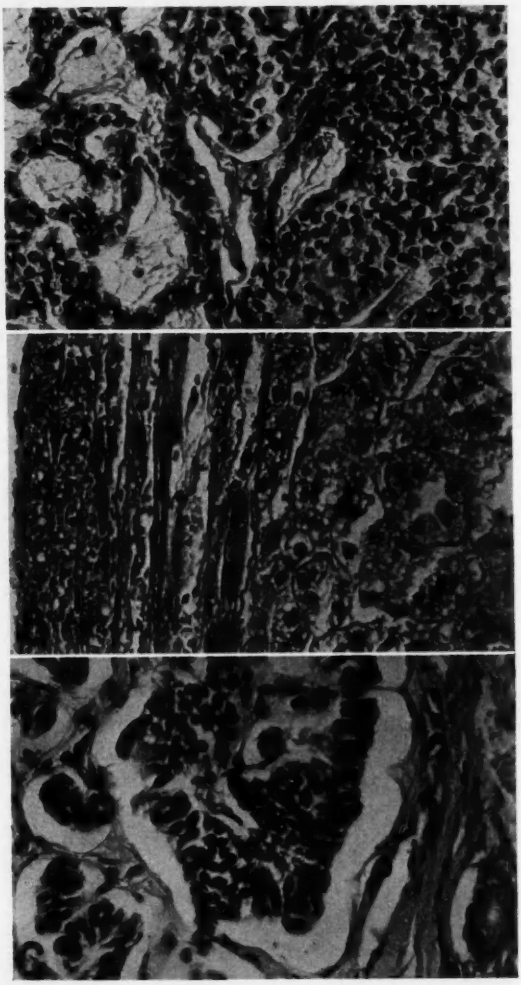

FIG. 3. *A*, case 4. Adenoma of parathyroid gland. *B*, case 4. Adenoma of adrenal gland. *C*, case 4. Adenoma of pancreas.

abdominal pains accompanied by occasional attacks of vomiting of 10 hours' duration, pains under each scapula.

Temperature 98 F, pulse 160, respirations 24. Blood pressure 109/90. Urine sediment was loaded with bacteria and a few pus cells. The leukocyte count was 9,500, hemoglobin 17 gm.

The diagnosis was acute peritonitis due to a perforated ulcer. Because of the patient's exceedingly critical condition, it was deemed wise not to operate upon him and he was treated expectantly. The patient died 8 hours after he was admitted to the hospital.

Autopsy performed by Dr. Hass revealed multiple duodenal ulcers, one of which showed a perforation and acute diffuse generalized peritonitis; adenomas of parathyroid glands, with hyperparathyroidism; adenocarcinoma of insular tissue with (?) hyperinsulinism, atypical; large multiple adenomas of the adrenal cortices; colloid adenomata of the thyroid gland; infection of left kidney.

Microscopic examination showed adenoma of the parathyroid glands. No calcifications were present in the kidney.

DISCUSSION

The 4 cases that form the basis of this paper all had a history of one or more operations for renal or ureteral calculi. In only 1 case were skeletal changes present. In every case where there is a history of previous operation for stone, passage of calculi, the formation of calculi in the opposite kidney, or the presence of renal calcification, the patient should be carefully examined for the presence of parathyroid disease.

The onset of hyperparathyroidism is insidious and its course progressive. The symptoms of hyperparathyroidism vary greatly. The principal evidences of the disease are lassitude, muscular hypotonia and weakness, especially in the legs with decreased electrical excitability. Gastro-intestinal symptoms, such as constipation, indigestion, anorexia, may be present.

The renal symptoms are the same as in any case of renal stone. There may be pain, nausea and vomiting, and blood in the urine. Recurrences are common. In many cases there is a history of one or more attacks of renal colic associated with the passage of calculi. The urinary calcium excretion is increased.

Since hyperparathyroidism with osteitis fibrosa cystica was established as a clinical entity by Mandl in 1925, the general assumption has prevailed that hyperparathyroidism was always associated with bone changes. However, Albright and his associates have been the first to call attention to the fact that renal calculi and renal changes were very much more important in hyperparathyroidism than the skeletal changes. All cases of hyperparathyroidism do not have bone changes and more and more attention has been called to the role of the parathyroids in renal stones.

Albright and his co-workers gathered 67 cases of proved hyperparathyroidism, and found that osteitis fibrosa cystica occurred in only a third of these, while in a second third mild and often insignificant degrees of skeletal involvement were found, and the remainder showed no evidence of osseous disease.

Cook and Keating in 1945 stated that at the Mayo Clinic between January 1943 and July 1944 there were 18 proved cases of hyperparathyroidism. In 4 of these the patients had bone disease and in 14 instances the patients had associated renal calculi.

Norris in 1947 made an excellent survey of the literature on parathyroid

adenoma which covered 322 cases. Of the 322 cases, 17 or 5.3 per cent showed parathyroid adenoma with renal lithiasis and/or renal calcification alone; and 101 or 31.4 per cent with associated skeletal and renal lesions. Only 1.5 per cent of the adenomas failed to produce any clinically recognizable skeletal and/or renal changes.

Cope in 1942 reported 67 proven cases of hyperparathyroidism. Renal stone was present in 47 of them.

In Chute's series of hyperparathyroidism 84 per cent of the patients had renal stones, and in a series of cases of renal calculus 3 per cent of them had hyperparathyroidism.

It is imperative that every case in which there is a history of recurrent or multiple calculi careful examination should be made for the presence of a parathyroid adenoma or hyperplasia. The most significant laboratory findings are hypercalcemia and hypophosphatemia; hypercalcinuria and hyperphosphaturia. The nonprotein nitrogen content of the blood is usually normal in the early stages of the disease, but is increased later when damage to the kidney takes place. The normal value for serum calcium generally accepted is 10.0 mg. per 100 cc plus or minus 1.0 mg. The normal value for the inorganic phosphorus is 3.5 mg. per 100 cc plus or minus 0.5 mg. The diagnosis of parathyroid adenoma must be definitely established before surgical operation on the parathyroids is undertaken.

Cook and Keating stated that in cases in which uncertainty persists as to the diagnosis, they frequently rely on the quantitative determination of the excretion of calcium in the urine while the patient is on a diet low in calcium, as suggested by Bauer and Aub. They place the patient on a weighed diet of 2,000 calories and 125 mg. of calcium each day. In a normal person the excretion of calcium per day in the urine is less than 100 mg. A patient with hyperparathyroidism generally will excrete more than 200 mg. per day. If the excretion is between 150 and 200 mg. per day, one should become suspicious of the presence of hyperparathyroidism.

The decision whether to remove the adenoma first or to operate upon the kidney stone may present a difficult problem. In the ordinary case, treatment should probably be directed toward the parathyroid adenoma. There may be exceptions to this in cases in which the patient has only one kidney with a superimposed infection, or in cases in which anuria is present due to complete obstruction by a stone impacted in the ureter.

Following the removal of the parathyroid adenoma the serum calcium level will drop to normal within 48 hours. One must bear in mind the possibility of tetany following operation on the parathyroids, which is the result of the change from hyperparathyroidism to a temporary hypoparathyroidism with development of hypocalcemia. D. Hunter in 1931 in 32 cases states that "latent tetany after operation was common and manifest tetany often occurred with marked variations in severity. It was fatal in 1 case only in which two parathyroid tumors were removed." The patient of Boyd, Milgram, and Stearns (1929) developed

latent tetany with hypocalcemia as low as 4.95 mg. per 100 cc of blood. The patient was relieved by parathyroid extract and a diet which contained much milk. There have also been other cases reported in the literature on latent tetany.

As stated in the beginning of this paper, it was the onset of tetany after a thyroid operation that started Erdheim on his monumental work on the parathyroid glands.

Only a few cases of acute hyperparathyroidism have been reported in the literature. The symptoms of acute hyperparathyroidism are vomiting, loss of weight, anorexia, bone pains, constipation, lassitude, increasing drowsiness and evidence of fever, tachycardia. In the absence of conspicuous renal or skeletal disease, a careful examination of the neck for parathyroid tumor should be made, together with an estimation of the serum calcium and phosphorus, and radiography of the kidneys.

Experimental parathyroid poisoning was first produced by Collip (1926). Hueper (1927) demonstrated metastatic calcifications in organs, such as the kidneys, lungs and stomach in dogs dying of acute parathyroid poisoning. Thomson and Collip (1932) described parathyroid dosage in animals which caused vomiting, anorexia, failure of the kidneys and death in a state of uremia.

Gutman and his associates in 1934 described the gastro-intestinal manifestations of hyperparathyroidism, namely, anorexia, nausea and vomiting, constipation, and epigastric pain. They stated that "while these symptoms may suggest the diagnosis of duodenal ulcer or acute appendicitis, they have been considered as due to the toxic manifestations of hyperparathyroidism." It is possible for the patient to have both hyperparathyroidism and ulcer as occurred in case 4 in my series.

H. Milton Rogers in 1946 reported 2 cases of probable acute hyperparathyroidism associated with duodenal ulcer. In the one case, the condition was due to an adenoma of the parathyroid gland, and there was metastatic calcification in the kidneys, lungs and small arteries. In the second case, the condition was due to generalized hypertrophy of the parathyroids and of supernumerary parathyroid glands with hyperplasia of the large, clear cell type. Metastatic calcification was found in the kidneys and the dura mater.

Rogers states that "when hyperparathyroidism and duodenal ulcers exist together, vomiting may be the manifestation of either one. However, if intractable vomiting occurs with duodenal ulcer in the absence of demonstrable gastric retention, it might suggest the presence of hypercalcemia and in turn hyperparathyroidism. This diagnosis is even more suggestive if the vomiting is aggravated by the institution or the continuation of an ulcer regimen with a diet high in calcium and phosphorus. Anorexia, when present, is in favor of hyperparathyroidism. The occurrence of muscular weakness and lethargy is secondary to the effects of hypercalcemia and, when associated with vomiting, may offer assistance in the diagnosis of hyperparathyroidism."

Rogers' 2 cases did not suggest osseous or renal disease during life. The pre-

senting symptoms in each were those of coexisting duodenal ulcer and probable hypercalcemia. Treatment for duodenal ulcer, including a diet high in calcium and phosphorus, produced in each instance an exacerbation of symptoms: nausea, vomiting, lethargy, prostration and azotemia. Metastatic calcification was present in the kidney in both cases and involved the lungs and arterioles in one case and the dura mater and lungs in the other case.

Smith and Cook in 1940 reported a case of chronic hyperparathyroidism and osteitis fibrosa, in which the patient died in the second of two crises of acute hyperparathyroidism with acute necrosis and calcinosis in the kidneys and pancreas.

W. A. Oliver in 1939 reported 2 cases of acute hyperparathyroidism, and Dawson and Struthers in 1923 reported the case of a man with a history of typical bone lesions of hyperparathyroidism, with multiple fractures, and while under observation had an acute syncopal attack and was admitted with collapse and a rapid feeble pulse to the hospital where he died soon after admission. Autopsy showed parathyroid tumor and extensive generalized calcification in the vessels, heart, lungs, stomach, kidneys, spleen and liver.

SUMMARY

Four cases of hyperparathyroidism and renal calculi are reported.

In 1 case death was probably due to hyperparathyroid crisis.

In 1 case a duodenal ulcer and adenoma of pancreas was found and adenoma of the adrenal gland.

All cases gave a history of previous operation for calculus before coming under observation.

In 2 cases a palpable tumor was found in the neck at the time the patients came under observation.

In 1 case (the fourth), the parathyroid lesion was found at autopsy.

In 1 case a palpable tumor in the neck developed after operation on the kidney for stone.

One case showed osseous changes.

The urologist should be on the lookout for parathyroid disease in all cases of renal and ureteral stone, especially in recurrent cases.

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DISCUSSION

DR. J. A. C. COLSTON (Baltimore, Md.): I would like to report a case of parathyroid adenoma studied this year, which has some unusual features.

The disease is rare, as Dr. Kretschmer has indicated, but it certainly is up to us to recognize these cases as soon as possible after they are seen, because the whole picture of the disease changes if the parathyroid adenoma can be removed.

This patient was 53 and had had a known diabetes for 7 years. He had been on a diabetic diet and was quite well regulated by insulin. Eight months before he was seen, he had painless hematuria, and x-ray showed bilateral renal calculi. A second attack of hematuria brought him to the hospital, again without symptoms.

His blood pressure was 160/85. Examination otherwise was normal. His urine showed pus cells, red cells, and an aerogenes infection, with a heavy growth of Staphylococcus albus. The laboratory findings were nonprotein nitrogen 48, sugar 124 mg., calcium 13.8, and phosphorus 2.2.

(Slide) This shows the right kidney with a large stone in the pelvis and the dilated ureter, with some small stones in this lower calyx. Here we see a peculiar calcification which extends from the region of the right kidney across the lumbar vertebra into the region of the left kidney.

First, we had some difficulty in interpreting this, which was rather unintelligent in view of the patient's story of diabetes. Here is the stone in the lower calyx of the left kidney.

It was decided to remove the stones from the right kidney, which was done through a pyelotomy. The larger one was removed through a pyelotomy, and the lower one by means of a calycectomy. Then, the diagnosis of parathyroid adenoma having been made by the chemical studies, a typical parathyroid adenoma was removed by Dr. William F. Rienhoff of the general surgical service.

(Slide) As Dr. Kretschmer said, it is a question of judgment when to take out the adenoma and when to operate on the kidneys. We thought it would be best to attack this right kidney first, which was done. This is simply the pyelogram showing the stone in the pelvis and the two lower calyces.

(Slide) This was the picture after the stones had been removed from the right side, and it still shows the calcification of the pancreas, it still shows the stone in the lower calyx. This film was taken after the adenoma had been removed, and it is hard to see here but it became obvious that the stone on the left side was disintegrating. We originally intended to attack that also by calycectomy.

(Slide) The stone disintegrated, and a small collection ended up in the lower part of the ureter, which was removed by ureteral dilatation and a sandy material obtained. Chemically these stones were calcium phosphate.

(Slide) This is the end result. No stones in the right kidney, none in the left

kidney, the calcification of the pancreas as before, and no evidence of stone in either ureter.

I am just showing this case because it is an unusual one associated with parathyroid adenoma, in that a definite calcification of the whole pancreas occurred associated with diabetes. I would like to ask Dr. Kretschmer if he has seen a similar picture.

I might say that at the present time, the patient is free from symptoms. The aerogenes infection still persists in the urine in spite of several courses of antibiotics.

Dr. David M. Davis (Philadelphia, Pa.): I am particularly interested to hear Dr. Smith's paper, because I was interested in another aspect of this subject some years ago.

In 1923, having read numerous conflicting accounts in the literature of the effects of staphylococcus on the reaction of the urine, I attempted to throw additional light on this by obtaining from the pathology department a hundred different strains of staphylococci which had been recovered at autopsy in various kinds of diseased conditions.

These were studied by growing them in a buffered medium containing urea and also an indicator. We did not attempt to measure the production of urease quantitatively; nevertheless, the method was a rough quantitative method, because the degree of color change in the indicator showed approximately the amount of urease produced by the organism.

Now, under those rather artificial conditions, and with organisms which by no means all came from the urinary tract, we found, if I remember correctly, that about seven or eight of the hundred showed some urease formation and only two showed the formation of appreciable amounts of urease.

I have wondered ever since what was the significance of this small number of strains of what appeared to be staphylococci, producing urease, when all of the others did not. Now, possibly, Dr. Smith is on the path to finding out what the real clinical significance of this fact is.

Dr. Linwood D. Keyser (Roanoke, Va.): The finding of urinary urease associated with urinary calculi and crystalluria as so well presented by Drs. Smith and McIntosh brings up the question of the value of urease in dissolution of urinary calculi. Two years ago I presented before this association experimental evidence that certain ferments, among them soy bean urease, accelerated the action of Suby's G solution upon calculi in vitro. A number of cases were presented in which these ferments were used with G solution in the successful dissolution of alkaline earth stones by retrograde irrigation. The present authors now show that urease is present in the urine and seems to be relatively abundant in patients with calculous disease.

In considering this apparent paradox we further realize that urine must contain a urea-splitting ferment. If we allow a specimen of normal urine to stand for 24 hours at room temperature, ammonia forms, alkalinization takes place and crystalline deposition occurs. This must come about from the splitting of urea by some enzyme, a urease, contained in the urine or introduced by air bacteria.

Again urea-splitting organisms such as the Proteus group must act through producing some form of urea-splitting enzyme, i.e. a urease. It is probable that urine, with and without infection, may contain a variety of enzymes such as urease or co-urease. The biochemists find a number of such enzymes and co-enzymes in various body fluids.

In the artificial irrigator we did find that Suby's G solution was much more effective, its solvent action speeded up, and made the stone dissolution more complete when enzymes were used in pretreatment of the stone. Of the enzymes such as papain, pepsin, ficin proteinase and urease, the latter in 0.5 per cent suspension seemed most effective. We therefore tried it clinically. Just what would have happened if the patient had had his stone bearing kidney irrigated with G solution alone and the enzymes omitted in the individual case, we do not know. Nevertheless we gained the strong impression that enzymes acted on the calculus in the kidney much as they did on the stone in the artificial irrigator.

From the experiments in vitro it was found that enzymes seemed to break up the organic framework of the stone. In retrograde dissolution we are constantly bathing the calculus with an acid solution and concomitantly are giving appropriate antibiotics to attempt the elimination of organisms, especially those of urea-splitting type. When from solvent action on the stone, an organic mucoid envelope forms on the calculus, further surface action of the G solution is prevented. By irrigating the pelvis with enzymes such as urease this organic envelope is destroyed, so that further action by G solution is made possible.

In general may I add that retrograde dissolution of stone is only occasionally successful and that the eradication of urea-splitting organisms after they have been present for some time, is most difficult. The procedure itself is quite a physical and psychological ordeal for the patient.

Dr. Kretschmer's paper is timely and important in stone study. We have now had 5 well established cases of hyperparathyroid disease, 4 of these with urinary stone. Their follow-up study over a period of years is of interest.

One, a middle aged woman, had a calculous pyonephrosis for which nephrectomy became necessary. A parathyroid adenoma has been present for some years, with persistent hypercalcinemia and hypercalcinuria. She has not found time to have the parathyroid adenoma removed as she is nursing a paralytic husband. There has been no recurrence of stone and the patient feels well.

A Philadelphia physician, whose case history was presented before this association several years ago, had many recurrent stones. His blood and urine studies were indicative of hyperparathyroid disease. Several pelviolithotomies and two operations for removal of parathyroid adenomas have brought his calcium phosphorus metabolism to normal, decreased hypercalcinuria and caused cessation of stone formation over a period of nearly four years.

A young woman of 25 years with extensive bone changes, palpable parathyroid adenomas, hypercalcinuria and hypercalcinemia had a stone in the lower left ureter. The parathyroid adenomas were removed with temporary return of the blood and urinary calcium values to normal. She refused operation for the

symptomless stone. We followed her over a period of 6 years during which time nephritis became progressive with ultimate death from uremia.

Two other cases have been diagnosed and treated during the past year.

In our stone work-up we make use of the Sulkowitch reagent almost routinely. If it is definitely positive, the patient is placed on a low calcium-phosphorus dietary such as that of Albright or Flocks. Then serum calcium, phosphorus, protein, and phosphatase determinations, together with study of the 24 hour elimination of calcium and phosphorus in the urine, are made repeatedly. This has led us to the diagnosis of hyperparathyroid disease on several occasions.

Hyperparathyroidism is not a frequent disease in Virginia or the South. Nevertheless it is a condition for which we must be on the alert and the routine application of the Sulkowitch test we believe of great value in this connection.

A final point may be made. Excessive calcium elimination in the urine may not be associated with hyperparathyroidism. Albright and Flocks have brought our attention to this fact. In many such cases the presence or absence of hyperparathyroid disease is controversial. We are led into a complexity of biochemical studies, which time and lack of immediate detailed knowledge on my part prevent me from entering into at present.

Dr. Thomas D. Moore (Memphis, Tenn.): In connection with Dr. Kretschmer's most interesting paper, I should like to ask if the stones in the 4 cases he is reporting all proved to be phosphatic.

Recently we unfortunately overlooked a parathyroid adenoma in a case in which a ureteral stone was removed by cystoscopic manipulation and chemical analysis of the calculus was reported calcium oxalate. For some time it had been our custom to study calcium metabolism only in those cases in which the stones proved to be calcium phosphate and in this instance estimations for blood serum calcium and phosphorus were omitted. Subsequently this patient was examined elsewhere and on finding evidence of hypercalcemia exploration revealed a parathyroid adenoma.

In another proved case of hypercalcemia secondary to a parathyroid adenoma in a young man aged 25 years, there was extensive calcinosis of one kidney, evidenced by punctate pericalyceal deposits of calcium. A right nephrectomy had been advised elsewhere on the presumptive diagnosis of renal tuberculosis. However, the operation was refused and my examination revealed that the process was beginning in the upper pole of the opposite kidney. Calcium studies disclosed a marked degree of hypercalcemia and at operation a parathyroid adenoma was removed. This patient has been seen at intervals for 7 years, during which time the calcium deposits have persisted and it may be assumed that they are permanent, but there has been no extension of the calcium deposits.

Dr. Edwin Davis (Omaha, Neb.): In Dr. George Livermore's paper, I was reminded of a young fellow we had, who lived along indefinitely and in good health, without symptoms, with two enormous calculi in the lower ureter, following nephrectomy. I told Dr. O'Crowley about this patient and mentioned that he had later taken an active part in college football, and Dr. O'Crowley said that he hoped he didn't get kicked in the stones.

DR. HENRY MORTENSON (Melbourne, Australia): With reference to Dr. Livermore's paper, I would like to relate to you a similar case, in which a patient had been operated on for stone in the ureter, and suffered a recurrence some months later. Operation to remove the stone on this occasion was unsuccessful, and nephrectomy was done and the stump of the ureter was left. He suffered hematuria and pyuria, and some 10 years ago consulted me. An x-ray at that time showed a stone 1.5 cm. by 1 cm. impacted in the lower end of the ureter. He did not want to have any more surgery. Since he was a short, stout gentleman with blue lips I wasn't very anxious to persuade him to be operated upon. He maintained the stone year in and year out, seeing me occasionally, with no increase in symptoms, and, with radiology performed once every year, perhaps, one could see the stone gradually increasing in size, until the last x-ray that was taken in this region, some 6 or 7 years after he was seen, showed a stone at that time the size of the forefinger, some 8 or 9 cm. by perhaps 1 or 2 cm. wide.

When I saw him some 12 months later, he said that the hematuria had cleared up. He had no acute manifestations or symptoms of any description, and the only reason for seeing me was that his symptomatology had changed to the extent that there was far more urinary irritation, coupled with a little difficulty sometimes in micturition.

He was submitted to x-ray investigation again, and, to our surprise, we found a large calculus, the size of a big hen's egg, lying transversely in the pelvis, obviously in the bladder. It was removed by cystotomy.

The interest of the case is, of course, that one could follow through the years the development of this calculus in the stump, and, furthermore, that the patient —and the surgeon as well—was fortunate in that he was able to get rid of it in this unusual and comparatively easy fashion.

DR. C. D. CREEVY (Minneapolis, Minn.): I would like to call attention to a simple maneuver which is useful when nephrectomy is necessary because of an ureteral calculus. One can, as soon as the kidney is out, pass a stone extractor (a Johnson basket or a Council extractor) down the ureter and extract the stone. While it won't work every time, it is quite simple and will save the patient an operation and the possibility of the complications mentioned by Dr. Livermore. If someone has already taken out the kidney, this method is not applicable.

DR. H. C. BUMPUS (Duxbury, Mass.): In connection with stones in the lower ureter, I would like to say that it is always a good idea to let the patient know the stone has been left in.

Some years ago, Dr. E. Starr Judd did a nephrectomy for pyonephrosis and, for some reason, the patient was not informed of a stone being left in the ureter. He came back a year or two later, under another name, and asked if we didn't believe that the surgeon who removed the kidney had made a mistake and that his kidney had been sacrificed when his real trouble was the ureteral stone.

Upon our disagreeing with him, although holding privately such a view, he became very angry, admitted his identity, purchased a revolver and went gunning for Judd. I notified the sheriff and he was picked up before any damage was done.

DR. HERMAN L. KRETSCHMER (Closing discussion): I, too, have left a stone in the lower ureter and have so informed the patient. There were no after effects.

It was interesting to have Dr. Livermore call attention to the fact that stones left behind in the stump of the ureter may at times cause trouble. I think we are apt to assume that because the kidney has been removed there will be no further trouble from the stones left behind.

In answer to the question about the chemical analysis of the stone may I say that the results will be published in the paper. I cannot give them to you accurately offhand. I will read them to you if you wish me to do so.

Some authors believe that if the blood chemistry studies are normal one may recognize early disease of the parathyroid gland by studies of the calcium elimination in the urine. There are equally as many men who disagree with that point of view.

In conclusion, I believe that we should bear in mind the possibility that there is this clinical picture and that we must recognize it early and not as happened in my series when three of the four patients had one kidney removed for stone with the development of a stone or multiple stones in the remaining kidney when the problem could have been solved by treating the lesion in the parathyroid gland.

PRESIDENT DEMING: We have two guests with us from Australia. I am going to ask Mr. Jose if he will rise, and Mr. Duff. (Applause)

TOTAL CYSTECTOMY FOR CANCER OF THE URINARY BLADDER

ROGER C. GRAVES AND (by invitation) WESTON T. BUDDINGTON AND ROBERT S. THOMSON

From the Urological Departments of the Pondville Hospital (Massachusetts Department of Public Health), The Carney Hospital and New England Deaconess Hospital, Boston

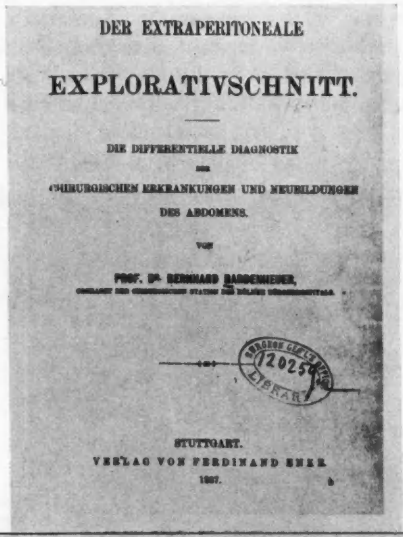
There has been a distinct tendency in recent years to broaden the field of cancer surgery and to combat malignant disease with more radical and extensive surgical procedures. Notable advances have been made and they have been possible largely through improved technique, more effective control of infection, better anesthesia and a more fundamental understanding of the physiological problems involved in a critical operation. The early diagnosis is still of paramount importance and the early lesion still offers the best hope of cure but great gains are being accomplished in the management of more advanced cases. We are learning that surgery must be just as drastic as it is necessary to be to cure the cancer, remembering at the same time to be only as drastic as it is possible to be and still leave the patient with life and good health.

Total removal of the urinary bladder has known a slow evolution and there have been three distinct phases in the development of this operation. In 1935, fourteen years ago, Dr. Edwin Beer wrote a book on *Tumors of the Urinary Bladder* in which he credited Bardenheuer with the first cystectomy in 1887 (fig. 1). Beer stated that Zuckerkandl collected 64 cases from the literature and estimated the general mortality to be 50 per cent. He quoted Young, who wrote in *Young's Practice of Urology*, published in 1926, that he believed the operation to be thoroughly unjustifiable. The disposal of the ureters seems to have constituted the principal problem in the early reports. Beer found that Papin had reviewed 181 cases of cystectomy and had concluded that the mortality of implantation into the intestines was 59.2 per cent. In Papin's collected series there were said to be 81 cases of transplantation to the bowel with 48 deaths. Beer performed cystectomy with signal success but it was his opinion that "the most satisfactory disposition of the ureters is made immediately after extirpation of the bladder by implanting the ureters into the skin of the iliac regions."

In view of such facts and opinions it is not surprising that total cystectomy was long regarded with general disfavor. There was little interest in an operation of uncertain outcome and doubtful benefit. The poor results that caused this attitude were due, as we believe today, to inadequate care and technique and especially to improper case selection. Cystectomy was a desperate last resort for those patients whose disease had progressed beyond the reach of ordinary forms of therapy and, too often, beyond the reach of any. We have had to learn that neither surgery nor any other agency yet available will cure advanced, widely disseminated carcinoma. The first cystectomy in this series was performed 17 years ago. The operator cannot remember having seen one before and he quite is

sure that he had never done one. The patient survived the procedure but succumbed within the year.

In the past decade or so, and these times are approximate, we have seen the second phase in the development of total cystectomy. There has been a new in-



DER EXTRAPERITONEALE

EXPLORATIVSCHNITT.

DIE DIFFERENTIELLE DIAGNOSTIK

DER

CHIRURGISCHEN ERKRANKUNGEN UND NEUBILDUNGEN

DES ABDOMENS.

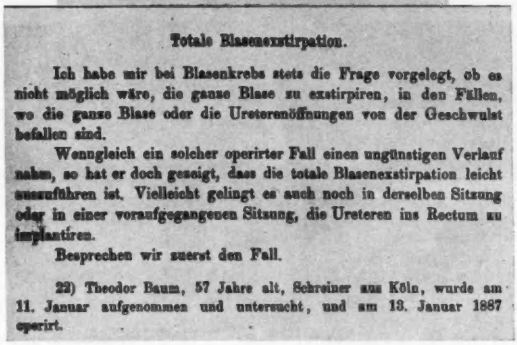
VON

PROF. DR. BERNHARD BARDENHEUER,

STUTTGART.

VERLAG VON FERDINAND ENKE.

1887.



Totale Blasenexstirpation.

Ich habe mir bei Blasenkrebs stets die Frage vorgelegt, ob es nicht möglich wäre, die ganze Blase zu exstirpiren, in den Fällen, wo die ganze Blase oder die Ureterenöffnungen von der Geschwulst befallen sind.

Wenngleich ein solcher operirter Fall einen ungünstigen Verlauf nahm, so hat er doch gezeigt, dass die totale Blasenexstirpation leicht auszuführen ist. Vielleicht gelingt es auch noch in derselben Sitzung oder in einer vorausgegangenen Sitzung, die Ureteren ins Rectum zu implantiren.

Besprechen wir zuerst den Fall.

22) Theodor Baum, 57 Jahre alt, Schreiner aus Köln, wurde am 11. Januar aufgenommen und untersucht, und am 13. Januar 1887 operirt.

FIG. 1. Photostatic copies of frontispiece and first page of paper containing description of removal of urinary bladder by Bardenheuer in 1887.

terest in this operation and it has become in this short period, one of the accepted surgical procedures for the treatment of bladder cancer. Cystectomy is being performed with increasing frequency and with increasingly encouraging results because of improved technique and because of more adequate preoperative and postoperative care in which the sulfonamides and antibiotics have helped immeasurably; and because of a wiser selection of cases.

The third phase in the evolution of cystectomy is quite recent. Those interested in this field now realize that to be a good cancer operation this procedure must include a radical and meticulous dissection in order to remove the regional nodes and lymphatic vessels in the iliac and obturator regions. This is now an essential and routine part of the cystectomy program. Until recently the importance of the extirpation of the regional nodes together with the bladder has been overlooked. Attention was centered upon the technique of the cystectomy itself and the associated problems of ureteral management. The greater number of patients are males, moreover, and an adequate gland dissection of the male pelvis was not easy. We have found that the procedure has been greatly facili-

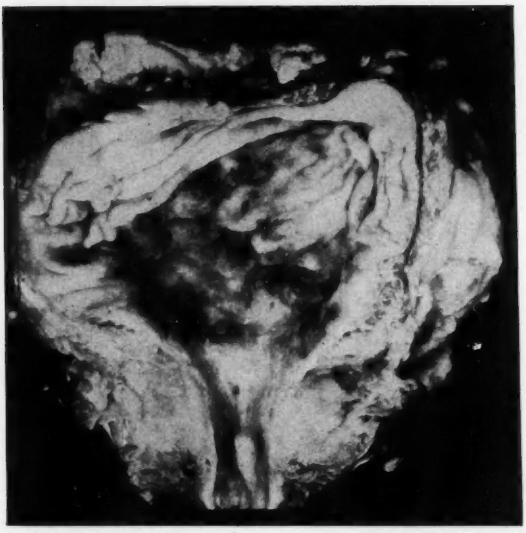


FIG. 2. Photograph of total cystectomy specimen. Pondville Hospital No. 20991. Infiltrating epidermoid carcinoma, grade 3, involving trigone. Whole prostate is shown to have been removed with bladder.

tated by the use of a transverse incision above the symphysis and extending outwards and upwards on each side as far as the anterior superior spine or beyond that point if necessary. Sometimes this incision is used alone and sometimes in conjunction with the vertical suprapubic incision formerly employed. In the transverse approach to the pelvis all muscle and fascial layers are divided at least on the side in which the spread of tumor seems more marked. It may be possible to spare a part of the rectus muscle and the deep epigastric artery on the other side and still obtain a good exposure of the extraperitoneal area. The incision may be carried high enough and the peritoneum may be retracted upwards sufficiently to permit the dissection of the gland-bearing fat along the common iliac vessels or even, as in a recent case, above the bifurcation of the aorta. With this approach a satisfactory and complete operation comparable to the Wertheim procedure for uterine cancer can be carried out. We agree that it is easier and more

effective when the whole cystectomy program is completed in one stage. If a ureteral transplantation to the bowel has been done previously, it is impossible to expose the iliac nodes at a high level on that side without the risk of disturbing the anastomosis. Because of this advantage we believe that the one stage procedure is likely to become more common in selected cases in which it seems safe to assume the added risk. A gland dissection at the time of a preliminary ureteral transplantation might be suggested, but we believe it to be unsound to remove the regional lymphatics before the extirpation of the primary tumor.

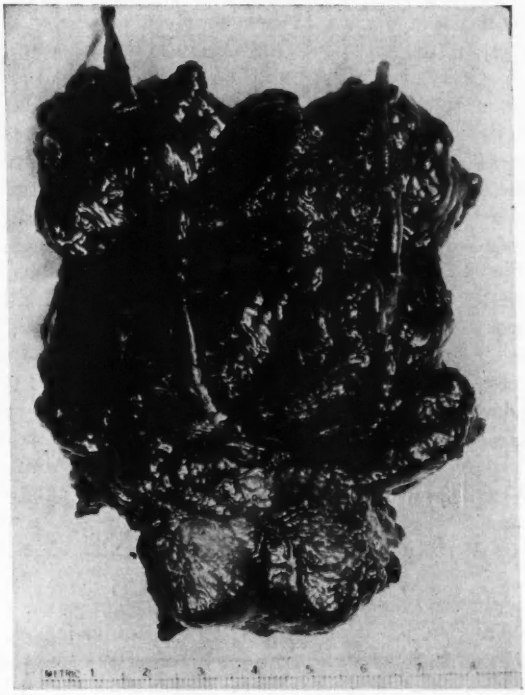


FIG. 3. Posterior view of bladder removed by total cystectomy. Carney Hospital No. 466989. Papillary carcinoma of bladder, grade 1. Prostate, seminal vesicles and vasa are shown to be included in specimen.

The indications for cystectomy are now clear cut and well recognized. In general, it is essential that the patient be in sufficiently good condition to withstand this extensive surgical program. Furthermore, cure should be impossible or unlikely by any less drastic treatment. The tumor must be confined to the bladder as far as it is possible to determine that fact. We do not believe in palliative cystectomies in the face of obviously inoperable disease. It is not palliation to prolong suffering. There is no analogy to be found in the abdomino-perineal removal of the rectum in the presence of known involvement of the liver. The

local symptoms of rectal cancer are usually more severe and more compelling than those of bladder carcinoma. The extirpation of the rectum is a simpler procedure. The patient with liver metastases may enjoy a significant extension of life and relative comfort. Death is too painful in the late metastatic stages of bladder cancer to justify an operation that cannot cure.

As far as the tumor itself is concerned, there are four indications for total removal of the urinary bladder: 1) Infiltrating carcinoma, always of indeterminate limits in the bladder wall, when it is so extensive that the visible or palpable growth within the bladder exceeds four centimeters at the most in its greatest diameter. Infiltrating carcinoma also, in most cases, when it has penetrated the whole thickness of bladder wall to produce a hard area that can be felt on rectal examination. Neither radium nor conservative surgery can be depended upon under these circumstances and in the case of the larger lesions of this type the amount of radium necessary to cure the disease would be greater than the bladder and the patient could well withstand. 2) Multiple papillomatosis, so-called, whether benign or malignant, in which so much of the vesical mucosa is infested by tumor that attempts to destroy the disease by radium or electrocoagulation will result in widespread fibrosis and serious impairment of bladder function. 3) Carcinoma of the trigone, especially infiltrating carcinoma, bordering upon or occluding both of the ureteral orifices. 4) Cancer adjacent to or involving the outlet of the bladder. It is doubtful that tumors so situated can be completely removed by methods other than cystectomy. Local excision or radium in sufficient amount, in this region moreover, are likely to produce obstructive changes at the bladder neck. We have stated in previous publications that carcinoma overlying the prostate is difficult to control with radiation. In a few instances we have followed the suprapubic electrocoagulation and radium treatment of small circumscribed lesions at the outlet of the bladder, with transurethral resection to remove the area of disease when the radiation reaction has subsided.

On the basis of these indications the selection of a favorable case for cystectomy is not difficult. The decision is not so easy in the border-line case of doubtful operability. Under such circumstances we must be concerned with human salvage and not with statistics and we must take the chance if the chance is a reasonable one. If we hold this attitude, and we believe that we should, the ultimate cure rate for total cystectomy for cancer may never be impressive because of the very nature of the problem with which we are dealing. By and large the favorable cases will do well, but some will be disappointing even in this group since we have no means of detecting microscopic metastases when the patient is studied or at the time of operation. There will be more frequent disappointments among the doubtful group but some will survive to justify the effort. Our own survival record, certainly not brilliant, is profoundly affected by this philosophy. We do not believe furthermore that cystectomy constitutes the only method of treating bladder cancer to the exclusion of other procedures; it is one of the methods and an indispensable one for those cases in which cure is impossible by other means.

For the new channels that must be provided for the urinary stream when the

bladder is removed there are three possibilities: nephrostomy, ureterostomy and transplantation of the ureters to the large bowel. Uretero-intestinal anastomosis is to be preferred when the condition of the patient and the state of the upper urinary tract are favorable. The results of this operation in properly selected cases are usually satisfactory (fig. 4) but not always so. Among our patients who have been operated upon for malignant disease, quite a few have come to nephrostomy, soon or late, temporary or permanent, but the operative mortality of the ureteral transplantation to the bowel need no longer be feared. It is an interesting

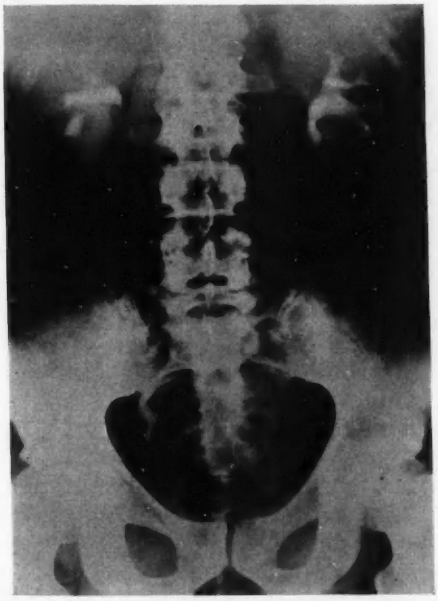


FIG. 4. Intravenous pyelograms nearly 6 years after total cystectomy and uretero-intestinal anastomoses. Pondville Hospital No. 16797. Epidermoid carcinoma of bladder, grade 1.

contrast that the mortality in 81 cases in the days of Papin was 59 per cent while in our series of about the same number of cases there have been 3 deaths, 5.7 per cent, and we have had no postoperative fatality since 1937.

We are discussing the whole problem of uretero-intestinal anastomosis in another paper now in preparation. There are certain considerations that should be mentioned, in connection with this operation however, when it is performed in association with cystectomy for cancer. We have had an impression, for example, that ureters which have been exposed to heavy radiation of the pelvic area do not function well when transplanted, probably because of changes produced in the ureteral muscle by endarteritis and fibrosis. It may be said, also, that we cannot recall a case in which nephrostomy or drainage of a ureter has become necessary after ureteral transplantation to the bowel in a patient operated upon for a non-

malignant condition. This seems to us to be significant and suggests the possibility, at least, that there may be influences in cancer patients which affect unfavorably the tone of the ureteral musculature or the normal reparative processes. We are all familiar, furthermore, with the frequent incidence of cases in which the tumor in the bladder has occluded the ureter on one side or the other with resulting dilatation. Prolonged dilatation leads to atony and atonic ureters cannot be depended upon to resume normal function and provide satisfactory kidney drainage after uretero-intestinal anastomosis. The disadvantages in this situation are increased if the dilatation is accompanied by infection. Finally, with reference

FIG. 5. Permanent nephrostomy in case of total cystectomy for epidermoid carcinoma, grade 2. Retrograde pyelogram made by injecting opaque medium through nephrostomy tube. Palmer Memorial Hospital No. 411984.

to methods of urinary drainage in association with cystectomy, we prefer nephrostomy to ureterostomy when conditions are not favorable for uretero-intestinal anastomosis, or when the results of the ureteral transplantation have been unsatisfactory (fig. 5).

The study of the patient should be the same in all cases of bladder tumor before a plan of treatment is selected. In addition to the physical examination and the usual laboratory investigations of the blood and renal function, there should be a chest film for further information about the heart and great vessels and to prove the absence of macroscopic metastases in the lung fields. Intravenous pyelograms are an essential part of the study. They give added evidence with reference to kidney function and reveal the presence or absence of ureteral or renal pelvis dilatation. A filling defect in the bladder in most instances denotes the size and position of the tumor, especially if antero-posterior and oblique views

of the bladder region are made. We cannot stress too much the importance of cystograms. They are particularly important in those cases in which cystectomy is being considered. Retrograde cystograms made with dilute dye through a small urethral catheter are often very much more revealing than those obtained by the intravenous method. It is distressing, as we have found in a few instances, to discover when the bladder has been removed that the apparently large tumor was really pedunculated and well localized and might have been dealt with by some less drastic procedure. This mistake can occur when a soft papillary tumor near the outlet of the bladder floats around the cystoscope in such a way as to give the appearance of an extensive annular growth. We believe that such a situation may be avoided usually by good cystograms and especially the oblique views which will show, in most cases, the extent of the base of the tumor (fig. 6)

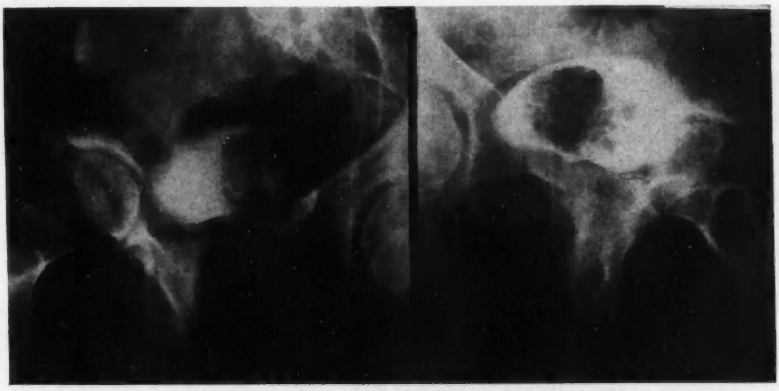


FIG. 6. Oblique cystograms. Palmer Memorial Hospital No. 1893. This tumor proved to be papilloma with 1.5 cm. base near left ureteral orifice. Favorable case for suprapubic electrocoagulation and radium. Cystograms often help in final decision concerning choice of treatment.

The cystoscopic inspection of the bladder should be carried out under spinal anesthesia. The relaxation of the patient and of the bladder, thus obtained, permits a better view of the tumor and a more accurate determination of its physical characteristics and its size and location. The relationship of the tumor to the ureters and to the outlet of the bladder must be carefully observed. As the bladder fills and empties one may be able to learn something of the extent of infiltration in the bladder wall. Some tumors near the vesical neck encroach so closely upon the urethra that the use of the pan-endoscope may be necessary to determine the presence of urethral involvement. At the time of cystoscopy a specimen may be taken for biopsy if desired. The fact and grade of malignancy do not influence very much the other methods of treatment but we advise biopsy in those cases in which cystectomy is contemplated because both the surgeon and the patient should have the support of this evidence before this radical operation is undertaken. We always fulgurate the site of biopsy to control bleeding and we always leave 10 per cent argyrol in the empty bladder at the close of these examinations.

Immediately following cystoscopy, and while the effects of spinal anesthesia

are still present, the rectal examination is made. Careful bimanual palpation of the whole pelvis and the region of the bladder, made possible through relaxation of abdominal and perineal muscles, is of the greatest value in the study of all cases of bladder tumor and especially in determining the suitability of a case for cystectomy. The degree of palpable induration in the bladder wall and its influence upon treatment and prognosis, as described by Jewett, should be kept in mind. Finally, and this is too often overlooked, the large bowel should be outlined by a barium enema before cystectomy and before uretero-intestinal anastomosis. We have had 1 case in which ureteral transplantation was decided against because of extensive colitis thus revealed.

We described our technique for total cystectomy in a paper presented before this association in June 1944. The chief addition to the material presented at that time consists of the regional node dissection already discussed. We would like to stress, also, the fact that cystectomy does not need to be an abdominoperineal procedure. We always remove all of the prostate and seminal vesicles together with the bladder in the male and the anterior vagina and most of the urethra in the female, through a suprapubic approach (figs. 2 and 3).

We have no fixed rules for cystectomy as far as the technical details of the operation are concerned. The order of procedure must vary with the needs of the individual case. It usually works out well to free the dome of the bladder first and the position of the tumor may require the removal of the adjacent peritoneum together with the bladder. When its superior portion has been freed it is usually easy to separate the bladder from the rectum by blunt dissection in the midline as far downwards as the seminal vesicles in the male. Next the gland dissection is carried out preferably on the side which seems to offer the greatest likelihood of spreading disease. As this dissection proceeds downwards from the common iliac level or higher the vascular attachments of the bladder come into full view on that side. These attachments are carefully divided. We do not hesitate to ligate the internal iliac artery if this will facilitate the dissection or reduce bleeding. In a recent case we have removed a section of the external iliac vein. The ureter is divided at a high enough level to escape disease and as low as possible to afford sufficient length for transplantation to the bowel or for ureterostomy. The same procedures are carried out on the other side. Sometimes, however, we divide the urethra next, distal to the prostate, and dissect the opposite side of the pelvis as the specimen is withdrawn. In approaching the urethra beneath the symphysis in the male, the puboprostatic ligaments are divided by sharp and blunt dissection until the prostate is well mobilized laterally and anteriorly. Two fingers are then placed over the apex of the gland like a fork or double hook and the urethra is divided between them with long scissors. The prostate is felt to give and to retract upwards when this division is complete and rectal injury is unnecessary. The proximal end of the divided urethra should be tied or clamped to prevent the escape of tumor cells from the bladder into the wound. The peritoneum is sometimes difficult to repair at the close of the operation and if so, we often use the sigmoid to help fill the defect.

We believe the after care following cystectomy to be of the greatest impor-

tance. The rectal tube which was introduced for a measured distance of about 6 inches before operation in cases of uretero-intestinal anastomosis, is left in position usually for 7 to 10 days. This must be kept open at all times to avoid rectal distention while the bowel is healing. Four drams of tap water are instilled through the tube every 4 hours, not as an irrigation but to insure its patency, and whenever there are signs of obstruction the rectal tube is removed and cleaned and replaced for the same distance. The tube should be dispensed with when the patient is sufficiently cooperative and recovers enough muscle tone to empty the rectum or when the bowel contents become too thick to drain freely.

Equal care is used in these cases to avoid abdominal distention until normal peristalsis is regained. The patient receives nothing by mouth except sips of water for moistening for the first few days and is then given a slowly increasing intake. Pantopon, grains one-third, or some comparable sedative, is given by the clock at four hour intervals. Wangensteen drainage is used, if necessary. In 2 cases we have attached gentle suction to the rectal tube. We commonly give penicillin, 50,000 units intramuscularly, every 3 hours by the clock, for the first few days after operation and withhold sulfadiazine until renal blood flow and diuresis have resumed normal levels. Parenteral fluids are given in sufficient amounts until peristaltic activity returns in the gastro-intestinal system.

The number of our total cystectomies performed to March 1, 1949 is forty-six; twenty-three of this number were patients at the Pondville Hospital while the remainder were from our private practice and were operated upon at the Carney Hospital and the New England Deaconess Hospital. The first operation was performed in July 1932 and although that patient has long since died, one of those operated upon the following year is still living but has recently developed carcinoma of the anterior vaginal wall, perhaps of uterine origin. In each case but two cystectomy was done for carcinoma of the bladder. The two exceptions were: a female patient with advanced cancer of the urethra and a 53 year old patient with adenocarcinoma of the prostate which had spread to the bladder, after 5 years of satisfactory endocrine control (fig. 7).

Thirty-five of the patients were male; eleven, female, the ages ranging from thirty-three to sixty-nine, with three in the third decade of life, eight in the fourth, twenty-eight in the fifth and seven in the sixth. Doubtless a few more patients in the older age groups will be chosen for this type of radical surgery as a result of improvement in technique and advances in the pre- and postoperative management. As was pointed out in the previous paper, physical age, which is primarily cardiovascular age, is more important than the calendar in the selection of such cases. We believe it will be unusual to find many individuals over seventy in whom life expectancy will warrant the considerable surgical risk involved.

SYMPTOMS

The symptoms noted in these patients were those commonly encountered in any individual with a bladder tumor, hematuria being the most frequent presenting complaint. The duration of this had varied from 1 week to several years and exceeded 6 months in nearly two-thirds of the group. However, there were

6 patients who had never observed bloody urine in spite of neoplasm extensive enough to warrant cystectomy. Six additional patients gave symptoms of bladder irritability rather than their hematuria as the reason for seeking treatment.

PREVIOUS TREATMENT

In evaluating candidates for cystectomy, knowledge of previous treatment is of considerable value because of its possible effects on the ureters in relation to their disposition, as an indication of whether the given tumor is radio-sensitive or not, and finally, as proof of failure to control the disease by measures short of radical extirpation. In our series, 10 patients had had varying amounts of high voltage x-ray therapy, one with million volt equipment. In a few instances the

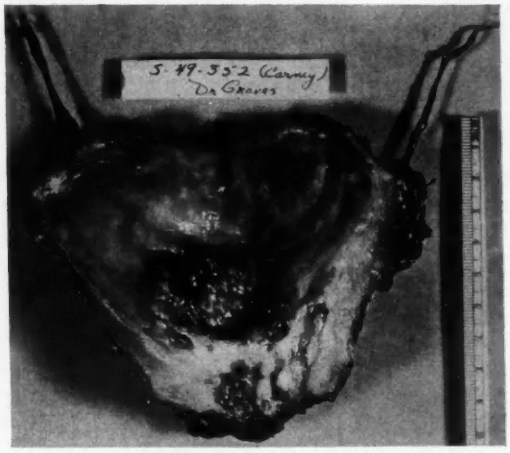


FIG. 7. Photograph of cystectomy specimen in case of carcinoma of prostate with extension to bladder. Carney Hospital No. 492578.

operation was somewhat more difficult because of fibrosis. As is common experience, delay in healing of wounds was noted in some of the radiated abdomens. We assume that the difficulty of pelvic adenectomy may be increased by previous radiation, as has been reported in like operations in patients with carcinoma of the cervix. One third of the total cases had been subjected, one or more times, to fulguration of the tumors by the cystoscopic or the suprapubic route; in 6 instances this had been combined with the implantation of radon seeds. Twenty-one patients had received no previous surgical treatment, and this group included all but one of the recent cases in which pelvic gland dissection was done as an integral part of the cystectomy.

EXAMINATION

Selection of cases after the routine studies have been completed depends to a major extent upon the findings by cystoscopic and rectal examination under spinal anesthesia. By the former, the type and site of the tumor are visualized

and by the latter, the question of fixation and extension through or beyond the bladder wall is determined. In thirty-eight of the series the tumor was not palpable on rectal examination or was limited to the bladder, while in six extension through the bladder wall or to the adjacent soft tissue had occurred. The 2 patients with carcinoma of the urethra and of the prostate are included in this latter group. In two instances no record of the rectal examination was available.

In general, the cystoscopic study has given us an accurate picture of the disease within the interior of the bladder. Occasionally a large papillary tumor whose base is near the outlet will surround the lens of the instrument and give the appearance of sphincter involvement when this is not actually present. Rarely, associated chronic inflammatory disease of the cystitis cystica type requires differentiation from submucous extension of neoplasm, and biopsy may be necessary to make the decision.

Based on the predominating type of tumor, our patients fell into three main groups: 1) The infiltrating lesions, which numbered twenty-two and were characterized by ill-defined borders due to the submucous spread of neoplasm. Even under direct vision with the bladder open, it is impossible to accurately define the limits of these tumors. For this reason we believe that fulguration and implantation of radon seeds will often give poor results in such cases, although the lesion may appear to be small. 2) The second largest group, numbering fifteen, consisted of the multiple papillary tumors. Some of these were subjected to cystectomy because of the large total area of mucosa affected, others because of their location around the bladder outlet. In the first instance treatment by electrocoagulation and the large doses of interstitial radiation required would have seriously impaired bladder function, and in the second instance, radiation of the bladder neck would not be well tolerated and in the case of prostatic involvement might be ineffective. 3) The third group included nine solitary but extensive papillary lesions whose bases were so broad as to require a prohibitive dose of radium, or whose site in relation to the trigone was such that occlusion of one or both ureteral orifices as a result of treatment seemed probable. Furthermore, there was danger that destruction of tissue in the trigonal area by coagulation and large doses of radium might give rise to perforation with the production of a vesicovaginal or vesicorectal fistula.

In keeping with one of the stated indications for cystectomy, viz. tumors in the region of the bladder neck, it is not surprising that thirty-six of the series involved the trigone or bladder outlet to a significant degree. In this connection it was found that impairment of the upper urinary tract as judged by intravenous pyelograms was present in twenty-four of the cases, seven on the right, eight on the left and nine bilaterally. The damage varied from mild dilatation of excretory passages to complete loss of function of a kidney, which had occurred in eight instances. Some of this injury to the upper urinary tract was the result of previous treatment and infection and not due solely to ureteral occlusion by tumor. Regardless of etiology, we were frequently confronted with the problem of choosing the best method of dealing with an abnormal kidney or ureter as part of the cystectomy program.

BIOPSY

In the majority of cases we have taken a cystoscopic biopsy of the lesion not as a primary method of diagnosis, but as a means of affording protection to both patient and surgeon in planning such a radical procedure. In general, the reports provided confirmatory evidence for the clinical diagnosis of cancer but presented no close agreement with the grade of malignancy as determined by the pathologist from the final specimen. This was true in twenty-nine of the 36 cases in which a record of biopsy was available and is in agreement with the work of Dean in this regard. In the seven remaining cases the biopsy was reported as benign papilloma in four when in reality carcinoma of grades 1, 2 or 3 was present, while in three carcinoma or papilloma was reported in the biopsy but no neoplasm was found in the bladder after its removal. We will discuss these patients in a later section. In another instance both the pathological report of the biopsy and of the operative specimen were papilloma, although at autopsy 5 years and 6 months later, metastatic epidermoid carcinoma of the para-aortic and inguinal nodes, liver, lungs and pelvic bones was found. No new focus of of cancer elsewhere in the body was discovered and it is therefore presumed that malignant disease of the bladder was present at the time of cystectomy.

The examination of the urinary sediment by the smear and stain technique of Papanicolaou was helpful in establishing a diagnosis in a few instances during the past 3 years. In 1 patient with an infiltrating lesion involving the posterior bladder wall the opposite was true, as both the urine and vaginal smears were repeatedly positive. A diagnostic currettage was performed and normal findings obtained. Subsequent examination of the cystectomy specimen consisting of bladder, uterus and adnexae revealed carcinoma limited to the bladder. This is the only instance we have encountered of a positive vaginal smear secondary to cancer of an internal urinary organ.

Another unusual case was that of a 57 year old man who sought treatment because of frequency and dysuria with hematuria. Repeated cystoscopic examinations by different observers revealed a bladder picture of diffuse inflammation more marked over the right postero-lateral wall where a few tiny ulcerations were seen. Because symptoms persisted after adequate chemotherapy, biopsies were taken and the report of epidermoid carcinoma was returned. Pathological examination of the cystectomy specimen revealed extensive carcinoma in situ. This case constitutes an excellent example of an unusual but dangerous inflammatory type of carcinoma of the bladder which simulates infection.

The final histological grading of the tumors brought them into three main groups: 1) epidermoid carcinoma, twenty-eight in number; one ungraded; five of grade I; eight of grade 2 and fourteen of grade 3; 2) papillary carcinoma, four ungraded; 3) transitional cell carcinoma, six ungraded. In addition there were 2 cases of benign papilloma and one each of adenocarcinoma, carcinoma simplex and carcinoma in situ. One prostate contained a separate adenocarcinoma apparently unrelated to the bladder tumor. Three bladders showed no evidence of tumor after removal, although two of these had had biopsies

reported positive for malignancy. All had undergone previous suprapubic operations with electrocoagulation and implantation of radon seeds, and it is believed that the inflammatory reaction secondary to such treatment was responsible for the error in clinical and pathological diagnosis. None of these patients had cystectomy during the past 10 years.

In the last year and a half we have carried out gland dissections of the iliac and obturator lymph nodes at the time of cystectomy in 8 patients; this was bilateral except in 2 instances. We believe there is no justification for a unilateral dissection except the poor condition of the patient precluding further surgery. In a ninth patient with carcinoma of the female urethra, bilateral radical groin dissection was done post-cystectomy. This patient and the one with adenocarcinoma of the prostate extending to the bladder were the only cases in which the pathologist found positive nodes. We have observed that the number of nodes reported in cystectomy specimens varies greatly with the persistence and skill of the pathologist and in our series has ranged from five in one instance to thirty-four in another. It is reassuring but may not be of great prognostic value to receive a report of many negative lymph nodes. In a recent specimen the pathologist stated that twelve negative nodes were found; the disease in this case was extensive and had penetrated the bladder wall to involve the adjacent peritoneum. Six months later the patient died of widespread recurrent malignancy.

Correlation of longevity with the grade of tumor agrees in general with similar studies for carcinoma of other organs. The total number of cases is small and no valid statistical deductions are possible. Of the 16 patients who succumbed to their disease, seven classified as grade 3 lived for an average of 13 months after operation. Three patients with grade 2 tumors and two with grade 1 tumors lived for an average of 25 months and 39 months respectively. Of the 3 patients with the so-called transitional cell tumors, one lived for 4 years, one for 3 years and 9 months and one for 4 months. One individual whose carcinoma was unclassified died after 1 year and 7 months. Of the 9 patients still living and free of disease for three years or longer, two had tumors of grade 3, three of grade 2, one of grade 1, one a papillary carcinoma ungraded and in 2 cases no tumor was found although marked radiation reaction was present. Three individuals who died from other causes and without disease 3 years or longer after cystectomy had tumors classified as grade 1, grade 2 and papillary carcinoma, ungraded, respectively—this last patient lived 7 years and 10 months following operation and worked daily until the time of his death.

SINGLE AND MULTIPLE STAGE PROCEDURES

Subdivision of the operation of cystectomy into two or more parts is made possible by the fact that the removal of the bladder and the diversion of the two urinary streams may be accomplished separately. An exploratory laparotomy to exclude metastases is always performed when the first abdominal incision is made. Recently it has been our policy to carry out the entire program as a one-stage procedure unless the operative risk was prohibitive. An analysis of the whole series reveals that 9 patients were thus treated. In three of the earlier cases bi-

lateral ureterostomies were performed at the time of cystectomy. One patient had a unilateral ureterostomy with ligation of the other ureter; another had a unilateral uretero-sigmoidostomy with ligation of the remaining ureter, and 4 patients had bilateral transplantations of the ureters into the large bowel.

Thirteen patients had two-stage procedures. The first part consisted of exploratory laparotomy and disposition of one ureter, while the second part included the cystectomy and disposal of the other ureter. Urinary drainage in these 13 cases was provided by ureterostomy in five, nephrostomy in four, and intestinal anastomosis in fifteen. One ureteral ligation was done on the side of a functionless kidney and in 1 case a kidney had been sacrificed several years previously because of tuberculosis. Actually 28 ureters were present in this group as one patient had bilateral reduplication. In this case we found the members of each pair loosely bound together by fibrous and areolar tissue so that they could be managed as one ureter and both bowel anastomoses were accomplished by the usual technique.

Twenty-four patients had their cystectomy program carried out in three stages. The first two stages included the disposition of the ureters and the exploration of the abdomen. A third operation was performed for the removal of the bladder. Although more of the multiple stage procedures were employed in the early cases, we have by no means abandoned the two and three stage plans for patients for whom one inclusive operation is unduly dangerous because of obesity, renal damage or inadequate cardiovascular reserve. The 48 ureters in this group were dealt with by ureterosigmoidostomy in thirty-four, nephrostomy in ten and nephrectomy for functionless or badly infected kidneys in four.

Even with complete study of the patient and his bladder as described, we have encountered an occasional case in which the preoperative choice of treatment between cystectomy and suprapubic cystotomy with electrocoagulation and interstitial radiation was still in doubt. Although we are reluctant to do so for fear of seeding the wound with tumor, the bladder has been opened a few times as part of the exploration to obtain more accurate information of the type and extent of the tumor. This has also afforded opportunity for additional examination of tissue by frozen section. The method has merit in border line cases. In one 50 year old man in good physical condition for whom cystectomy was chosen, we believe less radical surgery might have been performed had cystotomy with exposure of the tumor been carried out at the beginning of the operation. In another patient the plan for cystectomy was abandoned after the lesions were examined through the opened bladder.

COMPLICATIONS

The postoperative complications encountered in the series have been those which are commonly met with in any abdominal operation of comparable severity plus those complications more directly attributable to this procedure. The former were limited for the most part to pulmonary and cardiovascular lesions such as atelectasis, pneumonia and cardiac decompensation and on the whole were encountered infrequently. There was one abdominal dehiscence following a uni-

lateral ureterosigmoidostomy. There were 2 cases in which thrombophlebitis was recorded, fewer than one might expect in an operation confined almost entirely to the pelvis of elderly patients.

Complications specifically related to the operative procedures of cystectomy were primarily those of faulty urinary drainage and infection. Necrosis of the ureteral stump of a skin ureterostomy occurred in one instance and we have had three urinary fistulas, two of which were of brief duration and one urinary-fecal fistula; all were to the abdominal skin and all were secondary to bowel anastomoses which were satisfactory technical procedures. The causes, and points of origin, of these fistulas are not known. The convalescence in these patients was not otherwise abnormal.*

The impairment of renal function which may ensue with or without infection following transplantation of the ureters, requires constant vigilance to detect and correct, both during the immediate postoperative period and in the weeks and months that follow. We are discussing the subject as it relates to ureteroenterostomy in another paper. It is perhaps sufficient to say at this time that dilatation of the urinary passages of varying degree has occurred frequently in the early postoperative period of patients subjected to uretero-intestinal anastomosis. These changes have generally regressed in succeeding weeks as shown by decrease in the size of the excretory channels and increase in the concentration of the dye employed in intravenous urography. When the damage to the kidney proved substantial or progressive, especially if bilateral, we have performed nephrostomy as a safe and sure means of conserving renal function. Permanent drainage in this manner has been required after cystectomy in 4 patients, one bilaterally. Temporary nephrostomy drainage was employed in 10 cases because the bowel anastomoses did not function well at first; or because a safeguard for an infected kidney was required prior to uretero-enterostomy, or as an intermediate step in a planned nephrectomy. In 14 patients a permanent nephrostomy instead of ureterosigmoidostomy was chosen as the best method of diverting the urine of a kidney or ureter damaged by infection or obstruction. In 6 instances this operation was performed prior to cystectomy and in 8 cases, afterwards. In one of this latter group a previous ureterostomy had failed to provide a satisfactory solution.

We have accepted impotence in these patients as an unavoidable result of cystectomy. One vigorous man, now 52 however, who had his operation over 4 years ago inquired recently if there was any danger for him in sexual intercourse. Further questioning revealed that this function had been reasonably satisfactory though unaccompanied by the discharge of any ejaculate. We know of only one other such case, but have not included the subject in our follow-up examinations.

A few instances of other complications associated with the operation have been seen. In 3 patients marked edema of the leg resulted on the side of ligation of an external or common iliac vein, whose continuity had been interrupted to control hemorrhage, or to make possible the complete removal of adherent lymphatic

* Death occurred from chronic sepsis in the case of urinary-fecal fistula, after this paper was written. This reduces living patients to 18 or 39%.

tissue. In none of these cases did the disability prove serious. Two patients, both females, developed osteitis pubis as demonstrated by x-ray of the symphysis. In one of these pain on standing or walking was distressing for six to eight weeks; in the other, symptoms were confined chiefly to local tenderness. Recovery was complete in both patients with conservative treatment.

END RESULTS

Four postoperative deaths (8.7 per cent) have occurred in the series, but only one in the last 10 years. The first of these patients died of surgical shock directly after completion of the operation. In the second case death resulted primarily from coronary infarction but was accompanied by local peritonitis and prolapse of bowel through a dehiscence in the pelvic peritoneum. The third death was due to cardiac decompensation. The fourth patient, aged 60, died 6 days postoperatively of respiratory paralysis which the neurosurgical consultant believed to be due to thrombosis of the anterior spinal vessels in the cervical region of the cord.

Sixteen patients have died because of persistent or recurrent carcinoma. Six of these succumbed in from 4 to 10 months; seven lived for a period ranging from 1 to 2 years and three died at intervals of 3 years and 9 months, 4 years, and 5½ years after their cystectomy. Because of this considerable number in which all of the disease was obviously not removed, we reviewed the pathological report in each instance. In all of them large tumor masses were described, many of them grade 3. Thirteen of the sixteen cases showed either metastases to the regional nodes, or extensive involvement of the bladder wall with blood vessel or lymphatic invasion. One had a solitary brain metastasis at autopsy and in another the disease was confined to small pulmonary implants, death having resulted from coronary occlusion with infarction. None of this group with recurrent disease had pelvic lymphadenectomy as performed today. Probably the salvage would have been increased if gland dissections had been done, but a number of these patients, most of whom were operated upon prior to 5 years ago, would now be considered inoperable. As we have previously emphasized, however, in locally advanced cases without demonstrable metastases the attempt to save life must be made even though the results in such cases may be disappointing. For example, we saw recently a man of 58 who sought treatment because of hematuria of only 1 month's duration. Preoperative study and exploratory laparotomy revealed involvement of the entire left half of the bladder but no demonstrable metastases. A one-stage operation was done with uretero-intestinal anastomoses and gland dissection. Convalescence was unenventful and the patient was discharged in 21 days. At autopsy, less than 6 months later, a stony hard mass of recurrent tumor epidermoid carcinoma, grade 3, was present in the pelvis with innumerable malignant deposits throughout the abdomen and in the lungs (figs. 8 and 9). These are the cases that spoil the statistics but in such desperate situations, where disease appears to be confined to the bladder, the patient must be given the one chance of life afforded by radical surgery.

Seven patients died without evidence of cancer at the following ntervals

after cystectomy: 3 months, 7 months, 1 year and 4 months, 2 years, 3 years and 5 months, 3 years and 7 months, 7 years and 5 months. Two of these had had recent negative clinical examinations and the causes of death were said to be: 1) Perirenal abscess, uremia and pneumonia. The patient, Pondville Hospital No. 14962, had bilateral ureterostomies performed at the time of cystectomy in 1939. Later he had bilateral nephrostomies and still later, removal of the left kidney and a right uretero-intestinal anastomosis which never functioned well. He lived 1 year and 4 months after cystectomy. 2) Chronic pyelonephritis. The

FIG. 8. Intravenous urogram 5 months after total cystectomy and bilateral uretero-intestinal anastomosis for epidermoid carcinoma, grade 3. Fifteen minute film, showing slight dilatation of left renal pelvis and moderate dilatation on right side. Palmer Memorial Hospital No. 4542.

patient, Pondville Hospital No. 20304, had had a right nephrostomy in July 1943; cystectomy with bilateral ligation of the distal ureters in March 1944 and left nephrectomy in April 1944. He lived 3 years and 5 months after cystectomy.

Autopsies were performed in five of the cases in which death occurred without evidence of cancer. The final diagnoses were: 1) Pyelonephritis, bilateral. Pondville Hospital No. 4171. The patient had a suprapubic cystotomy with implantation of radon seeds for an extensive infiltrating epidermoid carcinoma of the left postero-lateral wall. Clinically the disease did not appear to be controlled. Bilateral uretero-intestinal anastomosis was performed followed by total cystectomy in July 1932. On pathological examination the bladder showed extensive radiation reaction but no tumor. The patient lived 7 months after cyst-

ectomy. At autopsy the kidney and ureters presented the picture of infection with slightly dilated pelves and ureters. Purulent urine could be expressed through the ureteral stomas into the bowel; the right orifice measured about 2 mm. in diameter; the measurement of the left orifice was not stated. 2) Thromboses of the aorta and coronary arteries; perforated duodenal ulcer; chronic pyelo-

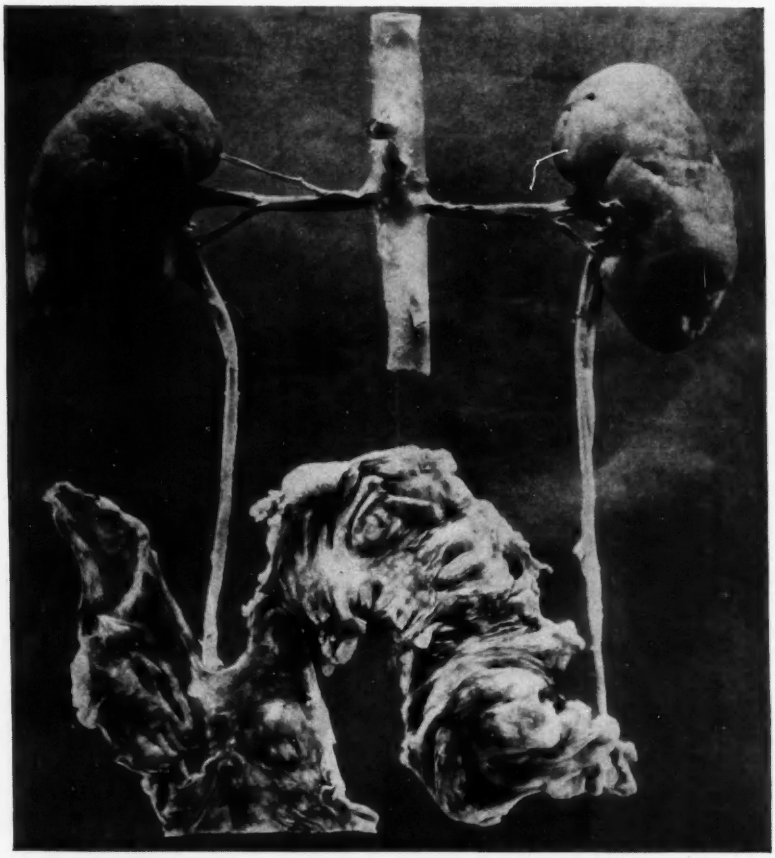


FIG. 9. Photograph of postmortem specimen 3 weeks after urogram shown in figure 8. Patient died from extensive metastases. Note satisfactory uretero-intestinal anastomoses and absence of significant ureteral dilatation.

nephritis, bilateral. This patient, Deaconess Hospital No. 37:1197, had million volt x-ray treatment totaling 8,000 r. for extensive epidermoid carcinoma of the bladder. Control of the tumor by this means was not attained. Bilateral uretero-intestinal anastomosis was performed followed by removal of the bladder in 1940. Because of repeated attacks of pyelonephritis, bilateral nephrostomies were done. The patient lived 3 years and 7 months after his cystectomy. 3) Bilateral

pyelonephritis. The patient, Pondville Hospital No. 12762, had bilateral ureterostomies performed at the time of total cystectomy for epidermoid carcinoma, grade 3, in 1937. Re-implantation of the right ureter to the skin was necessitated because of necrosis of the distal portion. He lived 3 months after cystectomy. 4) Pyelonephritis, bilateral; broncho-pneumonia. The patient, Pondville Hospital No. 23850, had a left uretero-intestinal anastomosis followed by implantation of the right ureter into the bowel at the time of cystectomy for epidermoid carcinoma, grade 1, in January 1946. Autopsy at another hospital is reported to have shown mild infection in the kidneys with dilatation of renal pelves and calyces, and marked dilatation of the ureters. A probe was said to pass readily through the anastomotic sites. The patient lived 2 years after cystectomy. 5) Ruptured aneurysm of abdominal aorta; bilateral chronic pyelonephritis. The patient, Pondville Hospital No. 15514, had a right uretero-intestinal anastomosis followed by a left nephrostomy prior to his cystectomy for papillary carcinoma in July 1939. Because of recurrent episodes of drainage from the suprapubic sinus for several weeks, the distal portion of the left ureter was removed and the proximal end ligated. At autopsy the right kidney presented changes of only mild infection and slight dilatation of the renal pelvis, calyces and ureter. A probe passed readily into the sigmoid. The left kidney showed considerable loss of substance and marked dilatation of the pelvis and calyces. The patient lived 7 years and 10 months after cystectomy, and the kidney which drained into the bowel survived better than the nephrostomized one.

Of the 19 patients still living, 41 per cent, six have been operated upon within the past 12 months. Five others are clinically free of disease for periods ranging from 1 year and 4 months to 4 years and 2 months and an additional six are known to be living and well from 5 years to 8 years and 11 months postoperatively. Two of this latter group have undergone secondary operations related to their original lesion. One had a nodule of metastatic epidermoid carcinoma of the same grade as his initial growth removed from his abdominal wall 5 months after cystectomy; this second operation took place over 7 years ago. In this patient a cystotomy to appraise the tumor was not done at the time of removal of his bladder but he had undergone previous suprapubic procedures which might have resulted in the implant. The other patient had a secondary operation which consisted of removal of the remaining urethra and the penis for papillary neoplasm of the proximal urethra occurring 7 years following cystectomy. The pathological report was papilloma. The original vesical lesion was epidermoid carcinoma, grade 1. It is now nearly 2 years since the second operation. Both of these patients were seen recently and no evidence of recurrent disease was elicited either by history or physical examination.

Two patients are alive 15½ years and 11½ years from the time of their cystectomy. The first, a woman, is now seventy-one. She had a suprapubic cystotomy with interstitial radiation and three courses of x-ray treatment each totaling 3200 r to the anterior and posterior pelvis prior to February 1933 for papillary carcinoma. Clinically the tumor did not appear to be controlled and uretero-intestinal anastomosis was performed on each side. A congenital hydronephrosis

on the right side gave some misgivings but did not cause trouble. Total cystectomy was done in September 1933. Pathological examination of the bladder revealed chronic inflammation but no tumor. Six years later a left pyelotomy was performed to remove a renal calculus and 7 years after that, or 13 years from the time of her uretero-intestinal anastomoses, a permanent right nephrostomy was done because of gradually diminishing renal function and the formation of another calculus in the left kidney. She has led an active life as a housewife and church organist and has been well through all these years. We were surprised to find on examination in the past few months a firm plaque of neoplasm in the anterior vaginal wall. Biopsy of this was reported as recurrent transitional cell carcinoma of bladder origin, although we suspect the possibility of a new tumor arising in the urethra or cervix.

The patient now living 11½ years after cystectomy is a man 56 years old. He had a suprapubic cystotomy with interstitial radiation and x-ray therapy totaling 1500 r to each of four pelvic portals for multiple benign papillomas prior to January 1937. A temporary nephrostomy was required because of infection in the right kidney with obstruction during the period of suprapubic drainage. Because of seriously impaired bladder function through contracture, uretero-intestinal anastomosis was performed on each side in preparation for total cystectomy in September 1937. Pathological examination revealed fibrosis and radiation reaction. The patient has led an active life and is now working as a hotel clerk in a neighboring city. At a recent examination in the clinic he appeared to be in excellent health and no evidence of disease was found.

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PELVIC LYMPHADENECTOMY AND TOTAL CYSTECTOMY IN THE TREATMENT OF CARCINOMA OF THE BLADDER[1]

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Cancer of the bladder continues to be difficult to cure. Past methods of treatment by fulguration, segmental resection and radiation were found to be relatively ineffective by the Report of the Carcinoma Registry in 1934 which showed that tumor recurrence followed such treatment in 46.2 per cent of all cases.[2] Three hundred and forty-nine cases of tumors of all grades and sizes in this report were followed for 5 years or more and, despite treatment, only 33.2 per cent of the patients were alive at the end of 5 years. Times may have changed since then but because of such reports as this and our own experience in the treatment of carcinoma of the bladder, we have adopted more radical methods of treatment. In 1945 and 1946, twelve total cystectomies and ureterosigmoidostomies for this disease were performed at the Massachusetts General Hospital while in 1947 and 1948, thirty-two of these operations were done.

It is fully expected that the successful total removal of the bladder will increase the number of patients cured of vesical malignancy. There is evidence, however, that even this radical procedure may fail to cure certain patients, even in the face of lesions which appear favorable. We have been considerably disturbed over the fact that three of 8 patients recently treated by total cystectomy at this hospital and followed for 6 months or more, have developed tumor recurrences in the pelvis. In none of these patients, at the time of operation, was there evidence of tumor extension beyond the bladder nor did pathological examination of the specimens provide such evidence. The most reasonable cause of failure of these cases seemed to be extension of the tumor into the pelvic lymph nodes.

At present, we do not know how frequently tumors which appear favorable for complete removal already have spread to pelvic lymph nodes, nor are we certain which lymph nodes are most likely to be involved. Examination of postmortem material of patients with apparently favorable lesions has suggested that lymphatic tumor spread is not at all unusual. Positive lymph nodes were present in 40 per cent of our own patients upon whom total cystectomy and dissection of the pelvic lymph nodes was performed. Since any malignant tumor of the bladder already may have spread to the regional lymph nodes by the time of operation, we now are removing, as thoroughly as we can, the lymph nodes of the pelvis in addition to total cystectomy.

Regional lymph node dissection has been an established procedure in surgery since Halsted[3] wrote in 1891: "About eight years ago I began to clean out

[1] This work was financed by the American Cancer Society.

[2] J. Urol. 31: 423–472, 1934.

[3] Halsted, W. S.: The treatment of wounds. Johns Hopkins Hosp. Rep. 2: 279, 1891.

the axilla in all cases of cancer of the breast." Taylor and Wallace reported that one third of patients with breast carcinoma, in whom positive lymph nodes were present, were alive and free of recurrence five or more years after radical mastectomy.[4] Gilchrist and David reported that 53.8 per cent of patients with carcinoma of the right colon and positive lymph nodes treated by radical resection were living and without recurrence five years after operation.[5]

With these facts as a basis, and with the background of the surgical treatment of malignant disease provided by Meigs, Taylor and Nathanson at our hospital, we believe that pelvic lymphadenectomy with total cystectomy is a reasonable procedure in the attempt to improve the number of cures of carcinona of the bladder. This procedure is performed easiest at the time of cystectomy. The only reference recommending such routine we have found is that of Godard and Kaliopulis in 1932.[6]

INDICATIONS FOR TOTAL CYSTECTOMY

Many factors bear on our decision as to whether cystectomy and ureterosigmoidostomy should be performed. First of these is the ability of the patient to withstand a formidable surgical procedure. The patient's age, physiological condition, and reasonable expectation of life without such serious surgery are considerations. Next in importance are the characteristics of the tumor.

Neoplasms of a high degree of malignancy as indicated by biopsy, tumors which are multiple and extensive, non-papillary growths in the lower third of the bladder, and tumors of any variety which have recurred after treatment, we believe usually are treated best by total cystectomy. The actual extent of the tumor, as estimated by bimanual examination, often is difficult to determine. Some degree of induration in the region of the tumor, or apparent fixation, may mean only a zone of protective fibrosis in advance of neoplastic tissue and does not necessarily mean inoperability. Thus, total cystectomy and pelvic lymphadenectomy are performed in cases where we believe the disease cannot, or has not, been controlled by less drastic measures and where we believe there is a reasonable possibility of eliminating the disease by these radical measures provided the patient appears able to withstand the procedure.

The absence of palpable lymph nodes in the pelvis at the time of exploration is no guarantee against lymph node involvement by tumor. In none of the 40 per cent of patients whose tumor had spread to the lymph nodes were nodes detected by palpation at the time of abdominal exploration.

PREOPERATIVE PREPARATION

Patients who are to have total cystectomy and transplantation of the ureters to the sigmoid are prepared as follows: Sulfathalidine gm. 8–10 by mouth daily for 5 days; streptomycin gm. 1.0 by mouth daily for 2 days; low residue diet;

[4] Taylor, G. W., and Wallace, R. H.: New England J. Med. **237**: 475–476, 1947.
[5] Gilchrist, R. K. and David, V. C.: Prognosis in carcinoma of the bowel. Surg. Gynec. & Obst., **86**: 359–371, 1948.
[6] Godard, H. and Koliopoulos, A.: La cystectomie totale chez la femme dans le cancer de la vessie. Rev. de chir., **70**: 201, 1932.

Miller-Abbott tube passed into the small bowel the day before operation; rectal tube left in place the morning of operation.

We have made little effort to clean the large bowel by cathartics or enemas except to irrigate the bowel through the rectal tube in the operating room until the return is clear.

The incidence of pulmonary embolism after total cystectomy has been sufficiently high, in our experience, to cause us to ligate the superficial femoral veins before operation as a prophylactic measure. When this precaution has been taken, there have been no deaths from pulmonary emboli.

OPERATIVE TECHNIQUE

Under endotracheal gas-oxygen and ether anesthesia, the abdomen is opened through a midline incision from the symphysis pubis to well above the umbilicus. The abdominal organs, the aorta, common iliac, external and internal iliac vessels are palpated. This procedure, as noted by Warren, "is an unreliable, though time-honored, guide in the determination of the presence or absence of metastases."[7] Experience has substantiated this observation.

The bladder is then examined. Usually, the tumor can be felt. If the mass is movable, we consider it removable. In cases where the tumor is located on the portion of the bladder covered by peritoneum, whether the latter is involved by tumor or not, the peritoneum overlying the tumor with a margin of at least two centimeters is left attached to the bladder. Peritoneal flaps are raised as shown in figure 1, *A*.

Starting at the lower end of the abdominal incision, the peritoneum is incised over the bladder so that an elipse of peritoneum 5 cm. wide and 9 cm. long is left on the posterior wall of the bladder. The incision then is carried down in the midline for about 6 cm. From this point, the peritoneum is incised laterally on each side to the point where the ureter crosses the common iliac artery. The ureters are left attached to the undersurface of the peritoneum medial to the lateral incisions. The peritoneal flaps thus outlined are dissected laterally from the perivesical fat until the external iliac arteries and veins are exposed from the femoral ring to the bifurcation of the common iliac vessels.

Dissection of the lymphatics starts by removal of fat and areolar tissue over the psoas muscle and is carried to the iliac vessels. All tissue surrounding the external iliac artery and vein is removed from the femoral ring to 3 or 4 cm. above the bifurcation of the common iliac vessels. Returning to the femoral ring, the dissection is continued medial to the iliac vessels and posteriorly, close to the pubic bone, until the obturator nerve is exposed. In most cases, this marks the posterior limit of the dissection. The obturator lymph node and the fatty tissue lying between the obturator nerve and the external iliac vein are freed. Lymph nodes present below the obturator nerve are included in the removal of the pedicles of the bladder. Lymph bearing tissue between the external iliac vein and the internal iliac vessels is dissected out along the branches of the internal

[7] Taylor, G. W. and Nathanson, I. T.: Lymph Node Metastases. Oxford University Press. New York, 1941. Foreword.

iliac artery and vein. The superior vesical artery is ligated and divided. The upper limit of the dissection of tissue along the obturator nerve and the lower

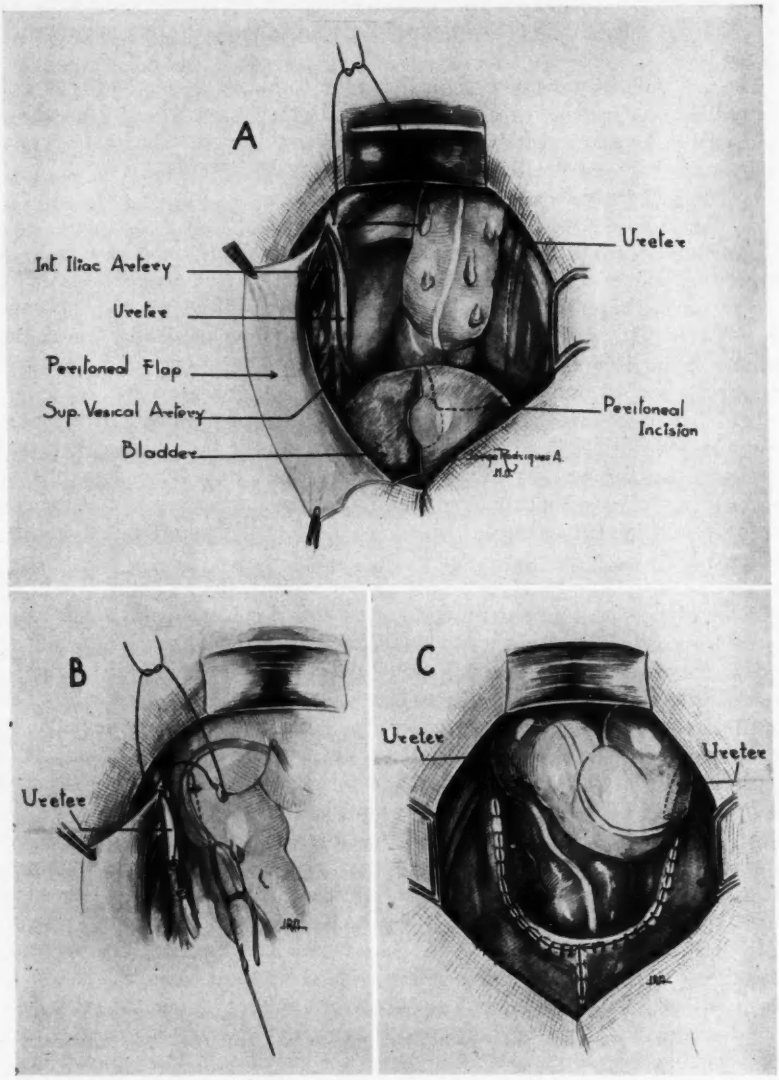

FIG. 1. *A*, incisions for peritoneal flaps; anchoring suture in sigmoid. *B*, right ureterosigmoidostomy. *C*, completed ureterosigmoidostomy; peritoneal flaps closed.

dissection of tissue along the branches of the internal iliac vessels are joined. Thus, lymph bearing tissue along the external, internal and along most of the

common iliac vessels, and tissue in the obturator space has been dissected en bloc and left attached to the bladder. A similar procedure is done on the opposite side.

Both ureters are divided about 4 cm. below the common iliac arteries. The vesical ends of the ureters are tied. The proximal ends are lightly occluded by bulldog clamps covered with shoelace to prevent urinary leakage. The loose tissue about the distal parts of the ureters is dissected and included with the specimen. The bladder is freed from the rectum or vagina and its pedicles clamped and ligated. The prostate and seminal vesicles are freed. The bladder is then removed through the abdomen or through the perineum after the abdomen has been closed.

Transplantation of the ureters to the sigmoid is done after removal or intra-abdominal freeing of the bladder. After trying several methods of ureterointestinal anastomosis, we have adopted the simplest possible technique. So far, this has been as satisfactory as more elaborate methods. The sigmoid is freed from the lateral pelvic wall if the mesentery is short. The sigmoid is drawn to the right and a cotton stitch is placed in the right mesenteric border of the bowel and through the posterior peritoneum just medial to the point where the right ureter emerges from behind the peritoneum. If there is any undue kinking of the sigmoid when this suture is tied, the suture is removed and placed where angulation of the bowel does not occur. The sigmoid is opened by a 4 mm. transverse incision in its wall anywhere in the antimesenteric border adjacent to the ureter as it first becomes visible extraperitoneally. The end of the ureter is cut off until there is bleeding. A catgut stitch is placed through the open end of the ureter and tied. The short end is cut. The long end is threaded through the opening in the wall of the sigmoid and brought out through the bowel wall 2 to 3 cm. below the incision. The ureter is brought into the lumen of the bowel and anchored by taking a bite of serosa and tying the catgut stitch. If the ureter and the end of a right angle clamp fit snugly, but not tightly, in the opening in the bowel, nothing more is done. If not, the opening in the bowel is enlarged or closed as necessary. A cotton suture is then placed in the left mesenteric border of the sigmoid at a level corresponding to the position of the suture in the right mesenteric border and is carried through the posterior peritoneum just lateral to where the right ureter emerges. This suture is tied if the sigmoid is not kinked by so doing. Thus, the sigmoid is rotated over the course of the ureter, which emerges from beneath the peritoneum and immediately enters the sigmoid. The left ureter is similarly transplanted. The virtues of this type of anastomosis, we believe, are: 1) the course of the ureter is not disturbed; 2) a good blood supply to the ureter as it enters the sigmoid is insured; and 3) there is minimal opportunity for scar tissue to form for only the thickness of the bowel wall surrounds the ureter and there are only a few millimeters between the edge of peritoneum and its entrance into the bowel.

The peritoneal flaps are closed and the abdominal wall is closed without drainage. If the bladder is removed through the abdominal incision a drain is left

through the urethra to the pelvis. If an abdomino-perineal operation has been performed, a drain is left through the perineal wound.

DISCUSSION

During the last 6 months of 1948, we have treated 10 patients with cancer of the bladder by total cystectomy, ureterosigmoidostomy and pelvic lymph node dissection. In 8 patients the procedure was done in one stage, though in one of these only the lymph nodes of the right side were dissected. Two patients had the procedure done in two stages. Although there were no operative fatalities, 3 patients died 24 or more days after operation. The others are well.

Positive lymph nodes were identified by microscopic examination in four of the 10 cases. This percentage might have been higher had we been able to have seria

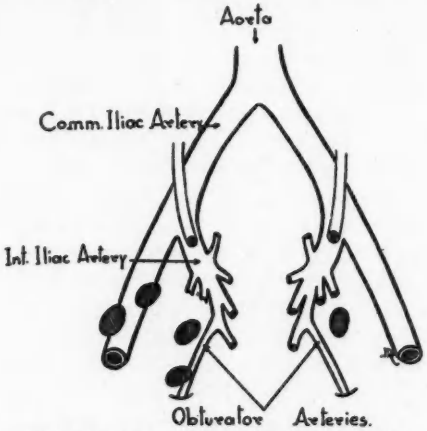

FIG. 2. Location of positive lymph nodes

sections made. Positive lymph nodes in these cases were as follows: two nodes along the right external iliac vessels, one node in the right obturator space, and nodes on both sides between the external iliac vein and the obturator nerve. The position of these positive lymph nodes is shown in figure 2.

To summarize, we believe that dissection of the regional lymphatics is a reasonable supplement to total cystectomy in the treatment of cancer of the bladder and that this procedure may increase the incidence of cure. It is recognized that in some cases of bladder malignancy, tumor cells will skip the pelvic lymph nodes and involve lymph nodes out of reach. Such cases, we believe, are not common. Although this operation is long and tedious, and in most instances is best done in one stage, mortality has not been excessive and postoperative complications have not been unreasonable.

CASE REPORTS

Case 1. (M. G. H. No. 621262) A man of 64 was admitted June 9, 1948. Six weeks previously, his bladder had been emptied of clot by cystotomy and a large

neoplasm partly excised. A solid 3 cm. tumor covered the left side of the trigone and occluded the left ureter. Tumor biopsy: epidermoid carcinoma grade 2. A left nephrostomy was performed but persistent bleeding from this kidney necessitated nephrectomy. Ten liters of blood were given the patient during his first 6 weeks in the hospital. On July 19, 1948, the bladder was removed by abdomino-perineal operation and the right ureter transplanted to the sigmoid. Pelvic lymph node dissection was postponed until he was in better general condition. On pathological examination, the tumor had extended through the bladder and invaded the left seminal vesicle. Six months later, after some persuasion, the patient consented to further operation and a retroperitoneal lymph node dissection was performed. There were two positive lymph nodes among those removed. One of these lay between the left external iliac vein and the obturator nerve. The other positive node was in the same situation on the right. The patient has done well.

Case 2. (M. G. H. No. 625225) A 75 year old man entered the hospital July 7, 1948 having had hematuria for 2 months. A large solid tumor covered the right side of the bladder from dome to trigone. Biopsy: Non-papillary carcinoma grade 2. On July 20, 1948 a right pelvic lymph node dissection, abdomino-perineal cystectomy and bilateral ureterosigmoidostomy were done. It was planned to remove the left pelvic lymph nodes later. On pathological examination, the neoplasm had penetrated the full thickness of the bladder wall and was graded 3. One lymph node of the right external iliac group contained cancer. This patient developed small bowel obstruction and 5 feet of tangled small bowel which had entered the unperitonealized pelvis were resected. Three weeks later he had a pathological fracture of the right femur and changes consistent with diffuse metastases were present in the lungs. He died a week later. Two days before he died, the nonprotein nitrogen was 44 mg. per cent. Post-mortem examination was not permitted.

Case 3. (M. G. H. No. 626870) A 63 year old man was admitted July 21, 1948 with a 6 months' history of hematuria. A large solid tumor, classified non-papillary carcinoma grade 1 by biopsy, covered the dome of the bladder. The mass was easily felt bimanually. On July 29, 1948, bilateral pelvic lymph node dissection, abdominal cystectomy and bilateral ureterosigmoidostomy were carried out. On examination, the tumor replaced most of the anterior wall of the bladder and extended into the perivesical tissues. Histologically, it was reported non-papillary carcinoma grade 3. One of the lymph nodes of the right external iliac group was positive for cancer. This patient recovered and has been well.

Case 4. (M. G. H. No. 494981) A man of 64 entered the hospital August 16, 1948 with a history of hematuria for 2 weeks. The bladder contained a large solid growth on the left wall and several smaller tumors on the anterior wall. These growths were non-papillary carcinoma grade 3 by biopsy. On August 20, 1948 bilateral pelvic lymphadenectomy, abdomino-perineal cystectomy and bilateral ureterosigmoidostomy were performed. On examining the specimen, it was found that tumor invaded the whole thickness of the bladder wall. None

of the lymph nodes contained cancer. Although it was necessary to retrieve a sponge left in the pelvis, the patient did well.

Case 5. (M. G. H. No. 600384) A 60 year old man was admitted August 23, 1948 for treatment of a recurrent tumor of the bladder. A so-called "non-malignant" neoplasm had been treated by suprapubic operation 5 years previously and again by segmental resection about 4 years later. At his last admission, there were three papillary tumors above the trigone graded papillary carcinoma 2. On September 13, 1948 bilateral pelvic lymph node dissection, bilateral ureterosigmoidostomy and abdominoperineal cystectomy were done. Histologically, the tumors were graded papillary carcinomas 2. None of the lymph nodes removed contained cancer. He has done well.

Case 6. (M. G. H. No. 538210) A 44 year old man entered the hospital August 13, 1948 with recurrent bladder tumors. In 1930 the left kidney, left testis and right epididymis were removed because of tuberculosis, and on his admission there was some evidence of Addison's disease. During the previous two years, multiple papillary tumors graded 2 and 3 had been treated by radon seeds on several occasions. Tissue removed from suspicious areas in the dome and anterior wall of the bladder was reported papillary carcinoma grade 2. On September 12, 1948, a bilateral pelvic lymph node dissection, right ureterosigmoidostomy and abdominal cystectomy were performed. The microscopic diagnosis of the tumors was non-papillary carcinoma grade 3. No cancer was found in the lymph nodes. His convalescence was uneventful.

Case 7. (M. G. H. No. 640217) A man of 54 was admitted October 27, 1948 with a 4 months' history of hematuria. The right side of the bladder was covered by a large solid tumor, necrotic in places. On biopsy, the lesion was non-papillary carcinoma grade 3. November 4, 1948, a bilateral pelvic lymph node dissection, bilateral ureterosigmoidostomy and abdominal cystectomy were done. The tumor involved all layers of the bladder and was reported non-papillary carcinoma grade 3. There was no involvement of the lymph nodes. The patient did well and was discharged in 16 days.

Case 8. (M. G. H. No. 463204) A 71 year old Negress was admitted November 1, 1948 with a recurrent bladder tumor. One year ago, a papillary carcinoma grade 2 had been removed by transurethral resection. Sections from the deep portion of her recurrent neoplasm were reported non-papillary carcinoma grade 3. In 1936, the patient had cerebral thrombosis resulting in spastic hemiparesis. Arteriosclerotic heart disease had necessitated digitalization for many years. The nonprotein nitrogen was 56 mg. per cent. Because of her precarious condition, bilateral pelvic lymph node dissections were done and the ureters were transplanted to the sigmoid November 15, 1948 but the bladder was not removed. Fifteen days later, however, her condition permitted total cystectomy and the removal of a segment of vagina adjacent to the tumor. The tumor was reported non-papillary carcinoma grade 3. The lymph nodes were not invaded. She did well for 12 days after operation and then died suddenly, apparently from cardiac disease since autopsy showed no other cause. Her ureteral anastomoses were widely patent and the kidneys were essentially normal.

Case 9. (M. G. H. No. 636416) A man of 75 was admitted September 25, 1948. Two weeks of hematuria was caused by a solid 4 cm. tumor on the bladder base, reported undifferentiated carcinoma. Since he did not seem a good candidate for total cystectomy, the bladder was opened and the tumor was fulgurated October 14, 1948. Five weeks later, it was necessary to close the unhealed cystotomy wound. His general condition then improved enough to warrant total cystectomy, although the nonprotein nitrogen remained at 45 to 50 mg. per cent. At the time of prophylactic superficial femoral vein ligation, adherent clots were present in the common femoral and iliac veins. These clots could not be removed by aspiration. December 7, 1948, a bilateral pelvic lymph node dissection, transplantation of the ureters to the sigmoid, and abdominal cystectomy were performed. The tumor invaded the entire bladder wall and was reported non-papillary carcinoma grade 3. His postoperative course was stormy with jaundice and general physiological imbalance largely due to pyloric obstruction. He died 24 days after operation. At post-mortem examination, there was a pulmonary embolus, pneumonia, endocarditis, pyloric obstruction due to a large malignant gastric polyp which had metastasized to the liver, and bilateral pyelonephritis. Both ureteral anastomosis easily admitted No. 8 ureteral catheters.

Case 10. (M. G. H. No. 641202) A 65 year old man was admitted November 15, 1948 for hematuria of 4 months. The bladder contained a large papillary tumor easily felt bimanually. Biopsy: papillary carcinoma grade 3. Bilateral hydronephrosis was present. December 22, 1948, bilateral pelvic lymph node dissection, bilateral ureterosigmoidostomy and abdominal cystectomy were carried out. The tumor had invaded the prostate and seminal vesicles and was reported non-papillary carcinoma grade 2. None of the twenty lymph nodes removed showed tumor invasion.

A review of the reported cases indicates that malignant disease was advanced in five, involving already the perivesical tissues. Pelvic lymph nodes were invaded by tumor in four of 10 patients. Three patients died after total cystectomy, pelvic lymph node dissection and transplantation of the ureters to the sigmoid, a mortality of thirty per cent. One death was from long standing cardiac disease, one from surgical complications and extensive tumor, the third died as a result of venous thrombosis and pyloric obstruction due to malignant gastric polyps.

SUMMARY

Past methods of treating carcinoma of the bladder, in the majority of cases, have failed to cure this condition. Recurrent disease, following total cystectomy suggests that even this procedure is, at times, an inadequate method of treating bladder malignancy. It is believed that bilateral lymph node dissection, in addition to total cystectomy, may increase the curability of this disease. This procedure is being carried out at the Massachusetts General Hospital in all patients considered suitable for total cystectomy. The indications for such radical surgery are outlined. Bilateral pelvic lymph node dissection, bilateral ureterosigmoidostomy and cystectomy in one stage is preferable, if the patient is considered able to withstand the procedure. A series of 10 patients is reported in whom these

operations were performed. In 40 per cent, positive pelvic lymph nodes were present on histological examination despite the fact that on abdominal exploration no palpable lymph nodes were present. A review of the reported cases shows that the operative mortality has not been excessive and that the immediate results have been reasonably good. A simple and quick method of anastomosing the ureters with the large bowel is described which, in our experience, has proved to be highly satisfactory.

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EXSTROPHY OF THE BLADDER: REVIEW OF 70 CASES

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Exstrophy of the bladder is a malformation which occurs in both sexes. In this condition the anterior wall of the bladder and the corresponding portion of the anterior abdominal wall are absent, so that the inner surface of the posterior bladder wall, bulging and everted, protrudes on the abdomen.

To quote Lower: "As this condition occurs about once in every 30,000 births and as there are about 2,000,000 births in the United States annually, about 70 cases should occur every year."

Exstrophy is encountered more frequently in the male than in the female, the ratio being approximately 7 to 1. In this series of 70 patients I have observed, 51 such irregularities occurred in males and 19 in females.

Unless children with exstrophy of the bladder are given the benefit of surgical intervention, 50 per cent die before the age of 10 years and 66.6 per cent before attaining the age of 20 years. There are no reliable statistics as to the number of children dying of secondary obstruction and renal sepsis during the first few years of life.

As may be anticipated, co-existing anomalies may be present. Such general malformations as harelip, cleft palate, meningocele or club feet may be observed.

In the male with complete exstrophy, epispadias and a short rudimentary penis are usually noted. It has been stated that complete exstrophy of the bladder in the male is always associated with a short rudimentary penis and epispadias. This belief was disproved recently when I observed a child with complete exstrophy of the bladder and a normal penis having an obstruction at the junction with the exstrophic bladder.

In 3 children in this series a double penis was noted, a small penis being present on each side inferior and lateral to the exstrophic bladder. A similar case has been reported by Lower. The scrotum may be normal or bifid. The testes may occupy a normal position in the scrotum or cryptorchidism may be present.

In the female the clitoris is cleft, the labia rudimentary, the urethra may appear as an open sulcus and a double vagina may be observed. The uterus may be normal, absent or bicornate. Pseudohermaphroditism was present in 1 case. Prolapse of the rectum was observed in 7 instances and atresia ani in 3 patients.

During the past 2 years 3 additional children have been seen in which the anus was absent; a pronounced prolapse of the rectum protruded from under the exstrophic bladder from 4 to 8 inches. The anterior wall of the rectum was absent, thus exposing the mucosa of the posterior wall of the bowel. These children were unable to walk because of pain of the exstrophic bladder and the protruding bowel.

It is generally agreed that the treatment of choice is transplantation of the ureters into the rectosigmoid and cystectomy. The preferable age for correction of this deformity has been given serious consideration.

As advocated previously, I believe the operation should be performed in infants during the first year of life for the following reasons:

1) If the operation is delayed many of the children die of urosepsis before attaining the age of 4 or 5 years.

2) Infants tolerate surgical procedures very well. This is attested by the results secured in operations for intussusception, hypertrophic pyloric stenosis and strangulated hernia.

3) As months or years elapse the lower third of the ureters frequently become

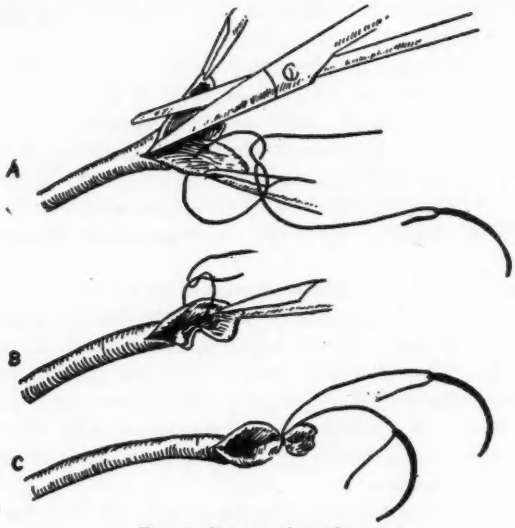

FIG. 1. Preparation of ureter

dilated by obstruction at the urethrocystic junction. This renders the operation more difficult or technically impossible.

4) The organisms in the bowel of infants are probably less virulent than in older children or adults.

5) When operation is performed at an early age, the children may develop normally both from the physical and mental standpoints.

6) The operative mortality and morbidity are low, while the end results are most satisfactory.

In a recent editorial, Counseller stated: "When one considers that from the statistical point of view half of these patients are dead by their tenth year and two-thirds are dead by their twentieth year, it simply indicates that whatever is done for them must be carried out before adolescence, and more particularly

before the tenth year." To quote further: "In recent years it has been recommended that these operations be done during the first twelve months of the patient's life under the supposition that an infant tolerates trauma unusually well and that the anomaly should be corrected before any recurrent renal infection develops. . . . Also this condition is not considered a surgical emergency, so one can conceivably wait until the fourth or fifth year when the anatomic structures are larger and the anastomosis can be more satisfactorily and accurately done."

Let us briefly review these considerations. As stated previously, 50 per cent of these patients are dead by their tenth year. This general consideration fails completely to consider the number of children that die of urosepsis during the first

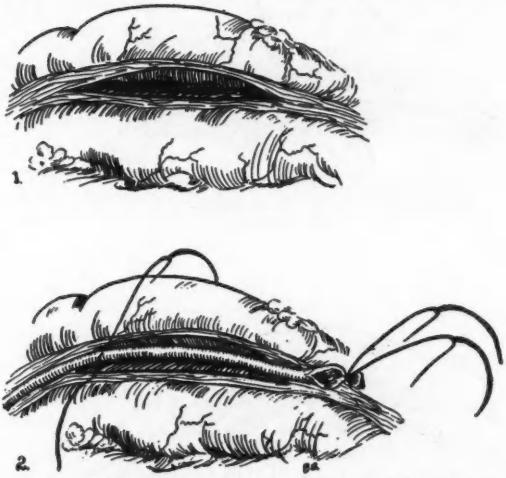

FIG. 2. Establishment of trough in rectosigmoid

four or five years of life. Certainly as evidenced and substantiated by vital statistics reports the 50 per cent of deaths does not occur between the ages of 5 and 10 years. Therefore many children will be permitted to die from a congenital lesion amenable to surgical intervention if the operation is postponed until the child is 4 or 5 years of age.

Second: It is true that surgical intervention for the relief of exstrophy of the bladder is not an emergency procedure. However, are we justified in permitting a congenital lesion to exist, which is conducive to the development of hydroureters, hydronephrosis, stasis, impairment of renal function, pyelonephritis and eventually death? Does this occur? I would like to present intravenous urograms of 12 children under the age of 4 years and you may judge for yourselves if postponement of the operation is to be advocated.

Third: The mortality and morbidity are low. It is true the operation is technically more difficult but surely this is no contraindication to performing the

operation in infancy. It is my observation that the most satisfactory end results to be secured are when the ureters are transplanted into the bowel during infancy. The ureters are of normal caliber and the kidneys are normal not having been subjected to repeated attacks of pyelonephritis.

In this series of 70 patients with exstrophy of the bladder the youngest child upon whom the operation was performed was 2 months of age. Twenty-two children under 1 year of age and a total of 33 under two years of age have had the ureters transplanted into the rectosigmoid and cystectomy. All of this group have

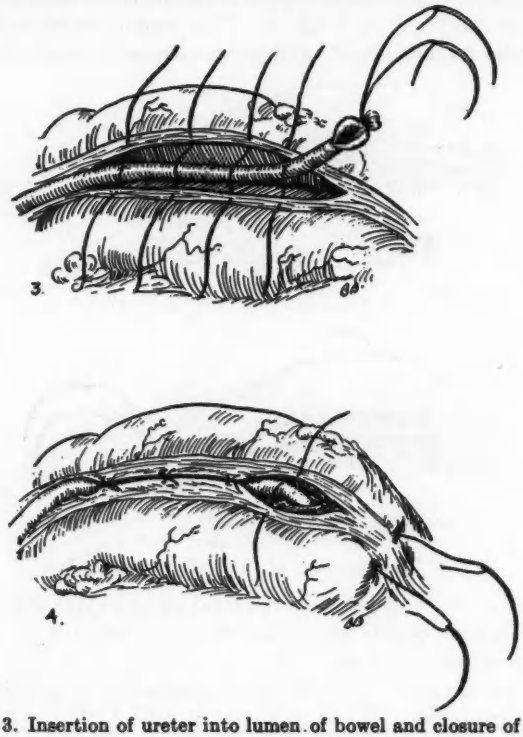

FIG. 3. Insertion of ureter into lumen of bowel and closure of trough

been discharged from the hospital in excellent condition. I therefore reaffirm my previous opinion that the operation should be performed during the first year of life.

The operative technique (figs. 1, 2, 3) employed is a modification of the Coffey I technique. In infants I prefer to transplant the right ureter first into the rectosigmoid. Ten or twelve days later the left ureter is transplanted and the bladder removed. In older children and young adults simultaneous transplantation of the ureters may be safely recommended. The plastic procedure for the correction of the epispadias is deferred until the child is older.

The ages at the time of operation were as follows:

	Cases
1–3 months	4
3–6 months	7
6–12 months	11
1–1½ years	7
1½–2 years	4
2–2½ years	3
2½–3 years	3
3–3½ years	1
3½–4 years	5
4–4½ years	1
4½–5 years	1
5–5½ years	1
5½–6 years	0
6–6½ years	1
6½–7 years	0
7–7½ years	1
7½–8 years	1
8–8½ years	0
8½–9 years	0
9–9½ years	2
12–12½ years	1
15 years	1
21 years	1
27–31 years	7
Total	63

MORTALITY AND END RESULTS

In this series of 63 patients on whom the ureters have been transplanted into the rectosigmoid and the exstrophic bladder removed, there have been 3 postoperative deaths. The remaining 60 patients were discharged from the hospital in satisfactory condition.

One child died shortly after the induction of ether anesthesia as the incision was being made in the abdominal wall.

The second child vomited his feeding 3 days following transplantation of the second ureter, and ceased breathing in a few minutes.

The third patient had an elevation of temperature to 106 F a few hours after operation and died the same night. There was no evidence of peritonitis and urine was passing into the rectum. A consulting pediatrician stated that there was a defect in the heat regulating mechanism.

Since discharge from the hospital 5 patients have died.

One patient died of uremia	20 months
One patient died during epispadias repair	2 years
One patient died, cause unknown	47 months
One patient died, cause and time indefinite	
One patient died of pneumonia	6 months

Of the series of 63 patients upon whom the ureters were transplanted into the rectosigmoid and cystectomy was performed, 55 are living and well, having been observed for periods ranging from 6 months to 15 years.

CONCLUSION

Transplantation of the ureters into the rectosigmoid and cystectomy are the procedures of choice for exstrophy of the bladder.

The operation should be performed preferably during the first year of life.

The mortality and morbidity are low and the end results most gratifying.

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THE UPPER URINARY TRACT FOLLOWING URETERO-INTESTINAL ANASTOMOSIS FOR BLADDER TUMORS

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The purpose of this paper is to describe the upper urinary tract following uretero-intestinal anastomosis for the treatment of bladder tumors. It is based on analysis of 99 consecutive patients operated on at the Memorial Hospital.[1] The Coffey I technique was employed on 97 patients, the end-to-side anastomosis was used on two. While uretero-intestinal anastomosis is used in the Memorial Hospital for treating suitable patients with cancers of the uterus, urethra, prostate, and vesicovaginal fistula caused by radiation, none of these patients are included in this group unless they also had bladder tumors. Four patients had bladder tumors with infiltration of the prostate. In one of these the primary tumor may have been in the prostate but it was uncertain. Two patients had primary tumors in both bladder and prostate.

In general, the operations performed prior to 1946 were done in two stages consisting of bilateral uretero-intestinal anastomosis followed in about 2 weeks by removal of the bladder and prostate through a combined perineal-abdominal approach in men, or abdominal cystectomy in women. Since 1946, with few exceptions, the operation has been done in one stage and has included removal of the iliac lymphatics with the bladder. In some instances an effort has been made to remove all lymphatics from the pelvis. This sometimes has necessitated a transverse colostomy and rectal resection with an end-to-end anastomosis. When advisable, the uterus and vagina have been removed.

Table 1, showing the duration of life of 99 patients following uretero-intestinal anastomosis for bladder tumors, gives a rough idea of the number of patients it was possible to observe at various periods after operation.

Of the 57 dead patients it will be noted that 27 succumbed within the first 6 months of operation. This group includes 20 operative deaths. These patients died from the usual complications of major surgery performed on elderly individuals. Kidney failure played a prominent part in but 5 deaths and even more rarely could kidney failure be attributed directly to postoperative ureteral obstruction.

Table 2 classifies 198 ureters and kidney pelves as they appeared in preoperative excretion urograms and at various periods after anastomosis with the bowel Elevation of blood urea nitrogen above a normal of 17 mg. per cent is also indicated in each group. It will be noted that before operation 137 or 69.5 per cent of the ureters appeared normal and that 22 or 11 per cent showed no more than a grade 1 dilatation. Only 11 or 5.5 per cent of the 99 patients showed retention

[1] These operations were performed by Doctors Marshall, Whitmore, Dean, and resident surgeons working under supervision. The series closed March 15, 1949.

of nitrogenous waste products before operation. In these individuals it reached an average amount of 21 mg. per cent.

Two weeks after operation, study of 124 ureters and kidney pelves showed a strikingly different picture. At this time only 12 or 9.6 per cent of the ureters examined roentgenographically appeared normal. Sixty-one or 48 per cent

TABLE 1. *Duration of life of 99 patients following uretero-intestinal anastomosis for bladder tumors*

	MONTHS										
	0–6	6–12	12–18	18–24	24–30	30–36	36–42	42–48	48–54	54–60	TOTAL
Living patients	13	7	5	6	2	4	2	0	2	1	42
Dead patients	27	10	8	8	3	1					57

TABLE 2. *Roentgenographic appearance of ureters before and after anastomosis*

	BEFORE OPERATION		TWO WEEKS AFTER OPERATION		THREE MONTHS AFTER OPERATION		SIX MONTHS AFTER OPERATION	
Normal	137	69.5%	12	9.6%	29	27%	24	42%
Ureteral or pelvic dilatation								
Grade 1	22	11.0%	61	48.0%	34	31%	11	19%
Grade 2	15	7.5%	31	24.8%	26	24%	8	14%
Grade 3	2	1.0%	8	6.4%	10	9%	7	13%
Grade 4	0	0.0%						
No evidence of function	18	9.0%	10	8.0%	8	7%	5	9%
Film not clear	4	2.0%	4	3.2%	1	9%	2	4%
Total	198	100.00%	124	100.00%	108	98.9%	57	101%
	Number of patients with elevated B.U.N. (over 17 mg. per cent), 11 or 5.5%		B.U.N. (over 17 mg. per cent) 20 or 16%		B.U.N. (over 17 mg. per cent) 15 or 13.8%		B.U.N. (over 17 mg. per cent) 9 or 15.3%	
	Average, 21 mg. per cent		Average, 35 mg. per cent		Average, 29 mg. per cent		Average, 31 mg. per cent	

showed a grade 1 dilatation, 31 or 24.8 per cent showed a grade 2 dilatation, while 8 or 6.4 per cent had reached a dilatation as great as grade 3. Twenty or 16 per cent of the patients, at this time, showed elevation of the blood urea nitrogen to an average of 35 mg. per cent.

Three months after operation, study of 108 ureters appeared to show a generally improved condition although loss by death of patients with dilated ureters may have improved the picture. Twenth-seven per cent of the ureters looked normal while 31 per cent showed only a grade 1 dilatation. Twenty-four per cent

showed grade 2 dilatation. At this time, 15 or 13.8 per cent of the patients showed elevated assays of the blood urea nitrogen. The average of this group was 29 mg. per cent.

Six months after operation, when only 57 ureters could be studied, the picture appears still more favorable because 42 per cent of the ureters looked normal, but the group is too small for significant analysis. Nine or 15.3 per cent of the patients

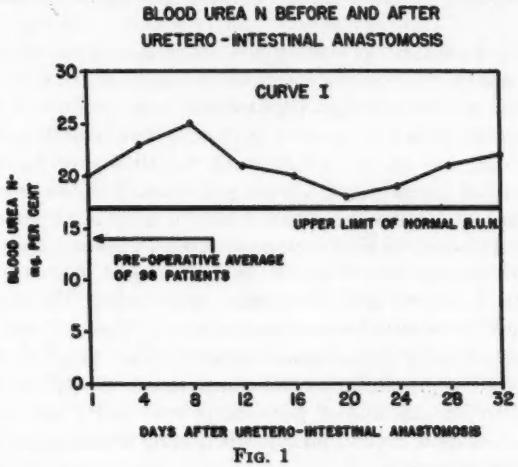

FIG. 1

TABLE 3. *Secondary operations required for correction of faulty uretero-intestinal anastomosis*

NUMBER URETERS TRANSPLANTED	NEPHROSTOMY	CUTANEOUS URETEROSTOMY	REIMPLANTATION IN BOWEL	NEPHRECTOMY
198	4 days..... 4 2 weeks..... 2 (1 closed) 6 weeks..... 1 1 month..... 3	1 week..... 2 2 weeks..... 2 1 month..... 1 2 months..... 1 2½ months..... 1 7 months..... 1	2 weeks..... 1 1 month..... 1 2½ months..... 1	3 months..... 1
Total..198	Total..... 10	Total..... 9	Total..... 3	Total..... 1

Total secondary operations: 23 or 11.6 per cent.

studied at this time showed elevated blood urea nitrogen. The average of these assays was 31 mg. per cent.

Figure 1 shows graphically the averages of blood urea nitrogen determinations taken before and at intervals of about every 4 days after operation.

It will be seen that the preoperative average of 98 patients was 14 mg. per cent. On the day following operation, the average was 20 mg. per cent. Four days later, it rose to 23, and on the eighth postoperative day reached 25 mg. per cent. From that point on, the average figure declined until 21 days after operation, the

average blood urea nitrogen assay was 18 mg. per cent. At this time, or sooner, the majority of the patients left the hospital, or their conditions being good, the tests were stopped. The assays recorded after the twenty-first day were from patients who were still definitely ill or who were slowly convalescent. These showed averages of blood urea nitrogen which rose on the twenty-fourth, twenty-eighth and thirty-second postoperative days to 19, 21, and 28 mg. per cent respectively. Because of diminishing numbers, further study was thought unproductive.

Table 3 shows the number of each type of secondary operation required for the correction of poorly functioning uretero-intestinal anastomoses. Of the 198 ureters transplanted to the colon, nephrostomy was performed on 10 kidneys; 9 ureters were transplanted to the skin; 3 ureters were reimplanted in the bowel, and it was necessary to remove 1 kidney. Of the 10 nephrostomies, 4 were performed 4 days after anastomosis; 2 were performed 2 weeks after anastomosis, of which one closed; 3 were performed 1 month after anastomosis, and one, 6 weeks after anastomosis. Of the 9 cutaneous ureterostomies, 2 were performed 1 week after anastomosis; two, 2 weeks; two, 1 month; one, 2 months; one, 2½ months; and one, 7 months after the original anastomosis. The three reimplantations in the bowel were performed respectively, one, 2 weeks; one, 1 month; and one, 1½ months following the original operation. The single nephrectomy was done 3 months after uretero-intestinal anastomosis. Of 198 uretero-intestinal anastomoses, therefore, 23 or 11.6 per cent proved faulty and were revised. It may be seen that in most cases a poorly functioning anastomosis was discovered early and rectified promptly.

COMMENT

Study of this material suggests that a certain degree of ureteral obstruction probably occurs regularly within 2 weeks of anastomosis. It is likely to result partly from surgical inefficiency and largely from tissue reaction. This ureteral obstruction may be shown roentgenographically in excretion urograms and may be reflected in increased retention of nitrogenous waste products. In favorable cases, these changes are temporary and the diameter of the ureters tends to decrease and the average of the blood urea nitrogen assays tends to diminish. When the ureters become seriously blocked or when kidney infection fails to respond to chemotherapy, secondary operations must be performed promptly. In this series 22 such emergencies were controlled by nephrostomy, uretrocutaneous transplantation, and re-anastomosis in the bowel. It was necessary to remove one kidney. Close clinical observation with frequent excretion urograms and measurements of the blood urea nitrogen assist one in performing these operations before kidney failure or infection reach a nonreversible stage. Since we followed this principle closely, operative deaths were hardly ever caused by ureteral obstruction, and of the patients who died after surviving surgery practically all succumbed to recurrent cancer.

This series is inadequate to permit detailed description of the upper urinary tract long after ureteral anastomosis with the bowel. However, in general, we

have observed that patients who survive a year do well except for recurrent cancer. Only one ureter required a secondary operation later than 3 months after anastomosis. Acidosis and pyelonephritis have occurred occasionally but, in all cases, have responded to medication.

While this presentation is concerned primarily with changes in the upper urinary tract subsequent to uretero-intestinal anastomosis, an operative mortality of 20 per cent must be deplored for many reasons, a minor one being the abrupt ending it makes to all further clinical observations. Although our operative mortality has lessened with practice, such extensive operations in patients who, on the whole, are elderly and ailing will always be considerable. It is unfortunate that for such a serious disease such radical surgery is required, but at present I know of nothing better when careful study suggests that more conservative measures are inadequate.

The fact that about 17 per cent of patients died of recurrent cancer within a year after they had survived extensive surgery suggests that either the patients were ill chosen because their disease was too extensive or the operation was inadequate. Unfortunately, at present, the most painstaking preoperative examinations of patients with bladder tumors frequently fail to show the true extent of the disease. Whether more extensive operations will provide a higher cure rate and, at the same time, preserve a useful individual is now being investigated.

This presentation shows the weaknesses of any statistical study made of individuals too few to have statistical significance. The subject appears, however, to have sufficient interest to warrant pooling of the observations of many clinicians by an agency such as the Tumor Registry of the American Urological Association.

SUMMARY

Study was made of the upper urinary tracts of 99 patients with bladder tumors before and after the transplantation of 198 ureters to the intestine. Before operation 69.5 per cent of the ureters appeared roentgenologically normal and the average assay of blood urea nitrogen for the group was 14 mg. per cent. Two weeks after operation only 9.6 per cent of the upper urinary tracts appeared normal while 72 per cent showed dilatation of grades 1 and 2. This ureteral obstruction, considered largely due to tissue reaction, was reflected in retention of nitrogenous waste products. As time passed, a tendency appeared for the upper urinary tracts to return to normal and for the elevated blood urea nitrogen assays to diminish.

DISCUSSION

DR. HUGH J. JEWETT (Baltimore, Md.): I consider it a great privilege to have been able to hear these most instructive papers that compose this symposium, but I should like to confine my remarks to the papers of Dr. Graves and Drs. Colby and Kerr.

There are two points that I should like to make, and I cannot make them with any great definiteness because of the small series of cases which we have accumulated up to the present time. There are, however, sufficient data, I believe, to convince us that these points are probably correct.

The first is that tumors which are superficially infiltrating have only rarely metastasized. The second point is that tumors which are deeply infiltrating have metastasized in a very high percentage of cases.

Previously, I had believed that the line of demarcation between the tumors with a high degree of potential curability and those with a low degree of curability should be drawn along the line of demarcation between the muscularis of the bladder and the perivesical fat; in other words, between groups B and C. But as time went on, we found that was wrong. The line of demarcation apparently should be drawn somewhere through the middle of the muscularis, roughly separating the muscularis into a superficial layer and a deeper layer.

Tumors which have infiltrated the muscularis superficially have behaved very much like the infiltrating tumors which have invaded only the submucosa. Tumors which have invaded the muscularis deeply have behaved very much like the tumors which have reached the perivesical fat.

We have 55 cases of segmental resection classified in this way, and 54 cases of total cystectomy classified in this way, making 109 cases in which the total local primary growth has been available for accurate section.

We have found that these two groups of cases have paralleled each other very closely. In the superficial group, less than half-way through the muscularis, the segmental resection cases have done even a little better, and I was distressed to hear that at the Massachusetts General Hospital that operation is considered outmoded. In the deep group, cystectomy will offer more in some of the cases.

Prior to November 1943, we had 57 cases done by cystectomy and by segmental resection, which have survived operation.

(Slide) That is a very small group, I will admit, but in this group that has invaded the muscularis only superficially, we had 12 cases, and 11 of those have lived 5 years or longer without recurrence. In the group that had invaded the muscularis deeply or had reached the perivesical fat, we had 45 cases and only 1 of those survived 5 years. I think by next fall, we will have one or two more, perhaps, if all goes well.

That indicates to me several hypotheses which we can not establish as fact as the series is too small; the first is that tumors which have not yet reached the half-way mark in the muscularis probably are, for the most part, strictly lo-

calized growths, and tumors which have gone beyond that point are not any longer confined to the bladder wall.

Now, if that is correct, then any procedure which is capable of completely destroying or eradicating a strictly localized superficial growth should be expected to result in cure. We know that total cystectomy and segmental resection both can do that. It is quite possible that other methods of treatment also can do that. We however don't know that yet because such cases have not been accurately classified clinically and segregated in this way before treatment. In time, I think we will have enough information to settle that point.

These cases that have gone less than half-way through the muscularis we cannot feel on pelvic examination under anesthesia at all. The biopsy taken of such a case may show infiltration in the muscle but careful palpation discloses no induration, no fixation, no thickening of the inferolateral ligament. The tumors that have gone more than half-way through the muscularis, on the other hand, practically always can be felt. We have yet to miss one, so far as I know. They always present a rubbery or an indurated mass.

Now, you can miss them when they are small and lie directly in front of the cervix uteri or when they are small and lie in the anterior wall behind the pubis but in other cases they can almost always be felt.

In regard to the deep cases, the ones that have gone more than half-way through, the question arises as to what should be done. These attempts to salvage patients who fall into this group by extensive gland dissection are laudable efforts, but I wonder actually how much, over a 5-year period of time, can be accomplished. In our autopsy cases, which had deeply invaded the bladder wall, 74 per cent showed demonstrable evidence of extravesical spread. Now we know that at autopsy microscopic metastases are many times missed, but 74 per cent of these cases showed demonstrable spread. Metastases therefore must have been present actually in a very high percentage of the cases.

Then, the excellent contribution of McDonald and Thompson showed, from a very careful study of their cases, that vascular invasion could be demonstrated when the tumor had reached the perivesical fat in nearly 50 per cent of the cases, and when it could be demonstrated, it was venous in about 40 per cent. Now, they leaned over backwards to be cautious and they refused to accept evidence of lymphatic invasion unless the perineural lymphatics were involved. We know that there are many lymphatics of the bladder wall that are involved that are not perineural in type. Again, they refused to accept evidence of blood vascular invasion unless they could see muscle in the wall of the vessel. Many blood capillaries are invaded by these tumor cells in which muscle is not present; so if they had made multiple sections of these tumors and had not confined themselves to such rigid criteria, I believe they would have demonstrated that the incidence of blood vascular invasion in this deep group is very high.

Such pathological observations as these should temper our optimism and should make us aware of the inherent limitations of extensive, radical surgery for deeply infiltrating cancer of the bladder.

Dr. William P. Herbst, Jr. (Washington, D. C.): Our whole conception of

surgery for cancer of the bladder is spectacularly changing year by year. Indications for operation are definitely changing, and it seems to me that possibly in attempting to arrive at a reasonable indication for operation, we might take arbitrarily a mortality of 10 per cent as a percentage which any surgeon would be willing to take in order to maintain a reasonable surgical policy.

As we go along with the additional assistance of good anesthesia and antibiotics and blood during surgery, in the way of support, our indices undoubtedly are going to change.

I don't think we should necessarily be moved too greatly by our ultimate cures in these cases. I think sessile infiltrating growths are nearly always in a group of cases which are almost bound to have metastasis by the time one makes the diagnosis, and ultimately, I think, the death is going to be due to malignancy. But from the standpoint of relief of suffering, we have another indication, and I think we have a good justification for surgery just for the terminal phases that a patient goes through who had extensive carcinoma of a sessile nature.

I would like, in closing, to ask the essayists, if they would, to tell us whether the death, in the majority of patients in whom they removed the bladder, was one of extreme suffering or just gradually going out.

I have 1 case that I want to present to you, of a uretero-intestinal transplantation in the case of exstrophy. (Slide) This was a boy, 10 years of age. This is an intravenous preoperative exploratory urogram, and you can see that there is very marked dilation of the ureter on both sides, very extended.

(Slide) This is a retrograde of the same patient, in which the lower ureter is very well visualized, and you will notice that the ureters are dilated well down to the exstrophic bladder, so that you have no opportunity to pick up a portion of the ureter where it may be of smaller count, in order to do a transplantation. The transplantation was done by the method described by Nesbit. I did this at Bethesda Naval Center, and they have done 6 other transplantations, using the same technique, and up to the present time, those 6 cases and this one are without mortality.

On the first postoperative day in this patient, the nonprotein nitrogen was lower than it had been before surgery. (Slide) This is 3 weeks after surgery, and I think there is some very slight suggestion of a narrowing of the ureters and of the renal pelves.

(Slide) This is 2½ months postoperative, and I think that that is very definitely a rather spectacular improvement in the degree of dilation of those renal pelves and the lower ureters, and we see the collection in the bladder.

This youngster is accommodating unusually well in that he is going to school and he will not empty his rectum because of his personal feeling in the matter, and because he has been a little sensitive of his social relationship to his classmates.

I want to present this simply to suggest that we have now a rather satisfactory method to employ in greatly distended ureters. I don't believe that we would be very successful in attempting to transplant ureters with that degree of dilation with our old technique, and, owing to the rather favorable course of this patient,

I thought it was well worth presenting in order to show what is possible, even with tremendously dilated ureters.

DR. LOUIS ORR, JR. (Orlando, Fla.): The Program Committee is to be complimented on the arrangement of these papers in the form of a symposium. Particularly, do I wish to compliment Dr. Kerr upon his very nice presentation.

Of recent date, we have had two patients who presented themselves with tumors on the anterior wall of the bladder. Associated with these tumors were hard involvements of what seemed to be inguinal nodes. Biopsy showed the identical histological tissue in the nodes (if they were nodes) as we found in the biopsy specimen of the bladder. This prompted us to look into the lymphatic supply of the bladder.

In going back to Keibel and Mall's work of years ago, beginning at about the mesonephros and tracing it all the way through, we come to the conclusion reached and stated in the last Gray's Anatomy, which is as follows—and I call your attention to the presence of nodes that I did not know existed, which have to do with tumors involving the anterior drainage: "The lymphatic vessels of the bladder originate in two plexuses, an intra- and an extra-muscular, it being generally admitted that the mucosa is devoid of lymphatics. The efferent muscles are arranged in two groups, one from the anterior and another from the posterior surface of the bladder. The vessels from the anterior surface pass to the external iliac nodes, but in their course, minute glands are situated. These minute nodes are arranged in two groups—an anterior vesical in front of the bladder, and a lateral vesical in relation to the lateral umbilical ligament. The vessels from the posterior surface pass to the hypogastric, external and common iliac nodes; these draining the upper part of this surface traverse the lateral vesical nodes."

These nodes, which I had no idea existed, may have something to do with these peculiar extensions of the malignant process, be they by lymphatics or by contiguity or continuity of tissue. We could not tell.

Two patients upon whom cystectomies have been performed during the past 12 months had, prior to death, developed metastases in these same nodes, which leads me to believe that there is something in the anterior pelvic wall, that is on the anterior wall of the bladder in the perivesical fat, to which we should give attention in our lymphadenectomies if we are to consider that we are going to perform a fair degree of total extirpation.

I have, in recent total cystectomies, employed two things which may be of some help, particularly to those doing total cystectomies in one stage. In two cases recently, to obviate the rather troublesome bleeding that can be encountered in the cul-de-sac, we have gone down as if we were going to do a retropubic prostatectomy, and ligated the dorsal veins of the penis; made a transverse incision through the capsule of the prostate and pushed it away as much as we could; then we proceeded posteriorly with the dissection. In the female, we have employed a two-operating team on those women who have tumors of the trigone. We simply operate above and below at the same time, taking out the entire anterior wall of the vagina and the urethra, joining very quickly. It makes the operation a very much easier situation.

I have had great difficulty, as I told Dr. Jewett before, in being able to differentiate between tumors which superficially infiltrate the muscularis and those which deeply infiltrate the muscularis, and we have found, in sectioning a few specimens from the bladder wall, that infiltration of the bladder tumor is not always on a level plane of infiltration. We have sometimes found that the tumor dips down quite deeply into the muscularis and then rises again into the submucosa.

The majority of our cystectomies had little success in prolonging life to any considerable extent. We have had too many female patients dying of pelvic masses after cystectomy, no doubt due to an inadequate lymphadenectomy, and too little respect being paid to the removal of the perivesical fat, which I think is extremely important.

I still say, as I think I said 9 years ago in this very place, that whatever procedure we use in the management of carcinoma of the bladder, it must be that procedure which is going to give the patient the greatest number of comfortable life years.

DR. GERSHOM J. THOMPSON (Rochester, Minn.): I want to discuss briefly Dr. Higgins' presentation.

Dr. Marvin Harvard, in completing his urologic fellowship, wrote a thesis on exstrophy of the bladder which involved study of the records of all cases seen at the Mayo Clinic with this condition prior to January 1947. He found 198 patients for whom this diagnosis was made out of slightly over 1,500,000 registrations. Of these, 134 were males and 64 females, a ratio of approximately 2 to 1 in contrast to the usually quoted ratio of 5 to 1. Fifty-four patients either refused surgical treatment or were treated by palliative surgery because the presence of severe renal damage made ureterosigmoidostomy an unwise procedure. The remaining 144 patients were treated by uretero-intestinal diversion of the urinary stream, the majority (133) by the Coffey-Mayo technique (with minor variations) as has been described in detail elsewhere. Moynihan's modification of Maydl's technique was employed in 1 case. The remaining 10 were one stage operations using the Coffey-Mayo technique of transplantation.

Of those undergoing operation the youngest was 10 months and the oldest 49 years of age. The preponderance of patients operated upon fell in the first and third decade with the former prevailing by two to one. Usually if the patient was presented in infancy the parents were advised to return with the child when it had learned bowel control—around 3 or 4 years of age.

Of the group of 144 undergoing ureterosigmoidostomy 123 were definitely traced by letter or were re-examined. The questionnaire sent sought information relative to the patients' general health, occurrence of pyelonephritis, and any further operations upon the urinary tract that might have been necessary. Four patients required nephrectomy a number of years after ureteral transplantation. Two of these had the procedure done at the Clinic and two had the operation elsewhere. A fifth patient returned to the Clinic for pelviolithotomy.

The incidence of pyelonephritis judged by response to questions regarding chills, fever and backache reveals 30 per cent who were free of such symptoms

and 70 per cent who admitted rare attacks or occasional attacks or in a few, fever as often as every 6 weeks. These febrile episodes were easily controlled by sulfa drugs or in recent years, penicillin.

Of the 144 patients undergoing operations, 41 had subsequent excretory urograms which were available for study. These were made any time from the first postoperative year (34 per cent) to the 35th postoperative year (1 case). The urograms were studied for evidence of urinary obstruction manifested by ureteral or renal dilation, nonvisualization and the presence of stones. An analysis showed that obstructive phenomenon of dilatation occurred with nearly equal frequency on each side, the left being slightly more frequently affected. Nonvisualization of the kidney was more predominant on the left but stone formation was predominant on the right. Of the 41 patients who had urograms 40 per cent had a normal right kidney and 30 per cent a normal left kidney. However, in only 12 per cent were both kidneys and both ureters considered within normal limits. In other words only 5 patients out of the 41 had a "normal" excretory urogram.

There were other interesting features brought out by the study of these urograms. Among them the point Dr. Herbst made that transplantation of the dilated ureter can result in a perfectly normal urogram later. So delay in operation until patients are through the diaper age does not always lead to a poor surgical result. We see very few of these patients in the first year of life. The records show that no child has ever been born in Rochester with an exstrophy, so unfortunately we do not see these patients as early as we might.

Regarding postoperative survival the study revealed that of the total 144 patients, 106 had "an opportunity" to survive 5 years or more, simply by virtue of having been operated upon prior to January 1, 1942. Of this group 98 were definitely traced and 85 or 86.7 per cent of the 98 patients had survived five years or more. Similarly of patients operated upon 10 years or more prior to 1942, 74 per cent of 85 traced patients were surviving; at 20 years, 52 per cent of 48 traced patients and four or 50 per cent of eight cases operated upon 30 or more years ago are still surviving. These results though far from perfect indicate the remarkable value in exstrophy of the bladder of uretero-intestinal anastomosis done according to the Coffey-Mayo principle.

Dr. Carl Aberhart (Toronto, Canada): I would like to show you two or three slides concerning uretero-intestinal transplantations done by one or two methods. In the absence of Dr. Nesbit, I would like to show you what results can be obtained by elliptical suture, and the speaker from Washington certainly verifies our experience in the results of this type of transplantation.

(Slide) These are just a few films which were taken out of a series of Coffey-type transplants, Coffey 1, done in our particular way. This is a preoperative film.

(Slide) This is a film taken 4 months after the transplantation, and you will see that he has some hydronephrosis and hydro-ureter on both sides.

(Slide) This is after a period of 8 months, with increasing hydronephrosis and hydro-ureter on both sides. The general experience I have had in doing Coffey transplants is that if hydronephrosis does develop, it is progressive and constant and does not return to normal.

(Slide) This, again, is a preoperative intravenous pyelogram.

(Slide) At the end of 4 months, poor function in the left kidney, some hydronephrosis and hydro-ureter on the right side.

(Slide) This is at the end of 8 months; no function in the left side.

(Slide) This is an interesting film in which I thought you might be interested. It is a preoperative pyelogram of a bilateral ureter with a complete obstruction, or practically complete, in his left side, enough getting through to give a pyelogram.

(Slide) This man was operated upon and a total cystectomy and transplant operation was performed. Both right ureters were transplanted by the Coffey method in two separate anastomoses. The left ureter was done by elliptical suture. This is at the end of 3 weeks.

(Slide) This is at the end of 8 months.

(Slide) And this is to demonstrate a further case, which I will talk about later on at the meeting. This is a patient with abacterial pyuria and chronic tuberculosis. The right kidney was removed on that diagnosis. You see the tremendous dilatation of the ureter. It was transplanted by elliptical anastomosis.

(Slide) This is the result at the end of 2 months.

I believe, on the question of transplantation, at the present time, that direct elliptical anastomosis offers more than any other method or type of transplantation.

Dr. Austin I. Dodson (Richmond, Va.): In view of the extreme rarity of exstrophy of the bladder, an experience that I had may be of interest.

About 3 years ago, I transplanted the ureters of two little boys, on the same date, because of exstrophy of the bladder. These children were attended by the same family physician and were both delivered by the same obstetrician within a week of each other, and at the present time, both are attending the same county school and taking part in all the activities of the little boys in that class.

They were four years old when I operated on them, not from choice but because at the time they were born, the obstetrician consulted a general surgeon, who likewise does some urology, and he advised him that after these children were four or five years old he could reconstruct their bladder. He did not think it wise to transplant their ureters. When they were four years old, he backed down, and they were referred to me.

One of them had dilated ureters at the time he was operated upon and still has dilated ureters, but excellent functioning kidneys.

My series of transplantations for exstrophy are, of course, nothing compared to that which has been reported, but of eleven patients, there has been only one postoperative death. Four of them are just about grown up, and one has had a baby under perfectly normal conditions and is very anxious for a larger family. As a matter of fact, she has refused to see me because she is afraid I will insist that she not have any more children.

I fully agree with Dr. Higgins that the sooner these children are operated upon, within reason, the better. The youngest upon whom I have operated was 2 years old. I have not seen them before, but I would not hesitate to operate

upon them much younger. One of these children, though 2 years old, weighed only about 16 pounds, because his mother said that because of his condition, she had spoiled him and he had been raised on potato chips and Coca-Cola.

DR. HERMAN L. KRETSCHMER (Chicago, Ill.): Many years ago I discussed with the late Dr. Edwin Beer the question of the proper disposition of the ureters when total cystectomy is to be carried out. He stated that he was not so sure that the transplantation of the ureters into the bowel was the proper procedure. He based his statement on the fact that too few patients had had this operation and that the time that had elapsed was not long enough for us to know what ultimately might happen to this group of patients. It was his opinion that it might be better to transplant the ureters into the skin.

For purposes of comparison it would be most informative if one could compare a definite number of patients who had transplantation of ureters into the bowel with a similar number who had transplantations into the skin. In this way we would have some factual data which would be of value in determining this question.

Enough time has now elapsed to make some of these studies and I am sure that each and everyone of us is grateful to Dr. Thompson for coming here and telling us of their experiences at the Mayo Clinic.

I would like to say a few words apropos of Dr. Graves' paper. It seems to me that great care must be exercised in patients who are to have a total cystectomy. I have seen many specimens removed for carcinoma of the bladder by means of cystectomy when grossly the specimen impressed me as one of benign papilloma of the bladder. Naturally this type of patient will have a perfect cure with a total cystectomy just as he will have with a resection and fulguration by means of the transurethral technique.

DR. JAMES T. PRIESTLEY (Rochester, Minn.): It is apparent from this excellent symposium on ureterosigmoidostomy and cystectomy that treatment of vesical cancer by complete removal of the bladder is receiving widespread and careful consideration. Unfortunately more time will be required before final answers are available for some of the problems and questions regarding this subject which still exist.

In this regard, one of the things that is still confusing to me relates to the exact indications for total cystectomy. From a theoretical point of view, one can speak with relative ease regarding indications; however, practical application of these theoretical considerations is not always so easy. In many cases decision for or against this procedure is not difficult. However, there are two groups of cases in which decision may be more difficult. One group is represented by the patient who has a relatively simple lesion which perhaps might be cured by a less radical measure. In other words, a choice must be made between segmental resection and total cystectomy. The prognosis afforded the patient by each of these procedures for a given type of lesion needs further clarification. The second group of patients in which the indication for total cystectomy is not too clear is represented by the patient who has an extremely extensive lesion perhaps with demonstrable extravesical extension. The prognosis for this patient over a 5-year

period after complete removal of the bladder should be more accurately evaluated. In my opinion, a procedure so radical as bilateral ureterosigmoidostomy and total cystectomy which may require some weeks of hospitalization seldom is justified as a palliative procedure when less extensive measures can afford relief of pain and discomfort during the patient's lifetime.

Dr. Kretschmer asked a question about the relative renal function after cutaneous ureterostomy as compared with ureterosigmoidostomy. Cook and Pool recently reviewed a series of patients that had total cystectomy for carcinoma. There were approximately 100 patients in this series. Fourteen of them had cutaneous ureterostomy performed and the remainder had ureterosigmoidal anastomoses established. Study of the postoperative urograms and pyelograms on these patients, taken at least 6 months postoperatively, revealed that of the 14 patients with cutaneous ureterostomy, 6 had normal pyelograms postoperatively. I cannot tell you for certain how many of these patients had abnormal pyelograms preoperatively, but I imagine they all did or cutaneous drainage of urine would not have been established.

In contrast, however, it was most disappointing to learn that a high majority of those who had ureterosigmoidostomy performed did not have entirely normal urograms postoperatively. That did not always mean, however, that renal function was significantly impaired.

(Slide) I have one slide showing the urograms on a patient who was a 31-year-old farmer, who had an exstrophy. I might say that we did not postpone his operation for that length of time as we had not seen him previously. As you see in the urogram on your left, there was definite dilatation of both ureters preoperatively. The postoperative urogram on your right was taken a few weeks after operation and it shows roughly the same situation.

I show this slide and the next one for two reasons: First, in my experience, the method which Nesbit has suggested for an end-to-side anastomosis between the ureter and the sigmoid has been quite helpful in these patients who have dilated and thickened ureters. That method was used in this case, and I have also used it in several other patients with at least early results that have been quite satisfactory.

(Slide) I show this slide because I have not seen anything exactly like this before. As you see, in the kidney to your left (that is his right kidney) there is quite a reflux of gas up the ureter, and I suppose that with wide-open anastomosis, this sort of thing may occur and possibly account for some of the pyelonephritis that these patients have; although, on the other hand, the differential pressure between the bowel and the urinary tract is not so great, I believe, but that if the opening is wide, reflux of this type ordinarily is not a serious matter.

I believe there is no doubt now that ureteral transplantation and cystectomy can be performed with a reasonable operative risk and that this procedure will be used more widely in the treatment of vesical neoplasm than in the past years. Satisfactory preservation of renal function can be maintained in most cases, and in others cutaneous diversion of urine can be established if necessary. More definite indications for cystectomy and evaluation of 5-year survival rates after

this procedure in comparison with less radical measures will be helpful in determining the exact place this form of treatment should have in the management of vesical carcinoma.

Dr. Roger C. Graves (Closing discussion): I have nothing to add. I have enjoyed these excellent discussions. I think that Dr. Orr has done a very useful thing to review the lymphatic drainage of the bladder. I thought Dr. Jewett's discussion was especially fine, but in spite of it, I think we have to go on trying. I enjoyed the papers of Dr. Colby and Dr. Kerr, Dr. Higgins, and Dr. Dean, and I listened to them with a great deal of pleasure and personal profit.

Dr. Fletcher H. Colby (Closing discussion): I would like in the first place, to have it definitely known that all of these operations were done by my resident, Dr. Kerr, who gave the paper. We have had others at the Massachusetts General Hospital but these are all his. He has done all of this work himself.

It is obvious that we have been trying hard to increase the number of patients whom we can cure of cancer of the bladder. I think we have made an advance in this, as evidenced by Dr. Graves' splendid paper on this subject. I, for one, refuse to take a defeatist attitude in this disease. I am sure that we have operated on quite a number of patients whose tumors have extended beyond the bladder and could not be cured by total cystectomy. However, our methods of determining that point are still quite inaccurate.

I feel that sometimes by manual examination and careful inspection of the tumor, we may not get the true picture. In some instances of bladder cancer where induration can be felt, the induration is not necessarily due to infiltration of tumor cells. It may be due to the protective layer of fibrosis that goes along ahead of cancer anywhere in the body, and some patients whose tumors seem advanced can be cured by surgery which is sufficiently radical.

The problem we have been concerned with has been to determine, in the first place, the incidence of metastases in the pelvic lymph nodes with patients who have bladder cancer, whom we think are suitable for total cystectomy and pelvic lymphadenectomy.

In the second place, we are trying to find out the actual location of the lymph nodes which are infected from this disease. I am sure that in some instances, lymph nodes will be involved that are beyond the pelvis. One such instance was a recent patient whose ureters I transplanted, and I was about to do a total cystectomy as a secondary procedure because he was a very severe cardiac. He died on the operating table under anesthesia, before the operation was started, of a massive pulmonary embolus. At autopsy, the tumor was limited as far as one could tell to the bladder. None of the pelvic lymph nodes were involved. One lymph node, however, up under the diaphragm, contained cancer. That will happen sometimes, in a few cases, but I am sure not in many, and even that will not deter me from being as radical as is consistent with the patient's chance of survival and well-being afterwards, in attempting to cure this disease which is notoriously very difficult to handle.

In this small series of cases reported by Dr. Kerr, involved lymph nodes in the pelvis were found in 40 per cent. Many of you will say that that is high, from your

own experience, and I am sure, or I feel reasonably certain, that with a larger number of cases, carefully observed and the lymph nodes carefully sectioned, we will probably find that 40 per cent is high. A review of these cases reported by Dr. Kerr will show that some of these tumors were rather advanced instances of malignant disease.

Although the incidence of pelvic metastasis in this disease may be low, I believe that total cystectomy and removal of the pelvic lymph nodes may cure a significantly larger number of patients than we can cure by total cystectomy alone. As Dr. Kerr said, we were considerably concerned over three recent patients upon whom total cystectomy had been performed, who returned with masses in the pelvis. None of these patients had had dissection of their pelvic lymph nodes, and it seemed quite reasonable that the spread had been by extension to the pelvic lymph nodes. These patients would have had a better chance of cure if these nodes had been removed, I believe.

As for the transplantation of the ureters to the sigmoid, the procedure we employ has been simplified as much as it is possible to do. These operations are long, tedious affairs, and any reasonable short-cuts that can be made are very helpful; so we have simply transplanted the ureter to the sigmoid in the simplest possible fashion.

So far, the results of this in our hands have been as good as any other type of anastomosis, and both ureters can be put in the sigmoid in this manner in 15 or 20 minutes.

Dr. Charles C. Higgins (Closing discussion): It is obvious that you cannot compare the end results secured today by transplantation of the ureters in the rectosigmoid with those reported years ago.

As all of you will remember, at our clinical society in Cleveland several years ago, I believe it was 11 years ago, that Dr. Lower reported either a hundred or a hundred and eleven cases that he had operated upon for exstrophy. In this series, 7 out of the first 10 cases died following operation. I am certain that there is no one in this audience who would have such an operative mortality. Certainly, that is not due to the skill and dexterity of the younger surgeons, but rather to our new chemotherapeutic agents.

We are in an era of conservation of renal tissue. I am certain that if any of you gentlemen had a child brought to you, a little girl, say, a year and a half old, undergoing attacks of pyelonephritis, you would not, on recognizing bilateral ureterocele, have advised that the child return in 5 years to have the ureterocele excised. You would have immediately excised the ureteroceles to restore the ureters and kidneys to normal.

The reason why most gratifying results are secured by transplantation of ureters in infancy is due to the fact that normal ureters are being transplanted. The kidney has not been subjected to repeated attacks of pyelonephritis. Obviously, if chronic pyelonephritis is present at the time the transplantation is performed, 60 or 70 per cent of these patients will continue at times to have attacks of pyelonephritis. Therefore, I state again, the operative mortality is low, the end results are excellent, and I believe that we should spare the upper urinary tract as much as possible in children with exstrophy of the bladder.

PRIMARY AMYLOIDOSIS OF THE BLADDER

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The true nature of amyloid disease is probably little better understood today than in 1893, when Wichmann first classified amyloidosis into the local and generalized forms. He recognized that a certain number of these cases showed localized amyloid in the absence of preceding debilitating disease; in other words, a primary amyloidosis. The amyloid in this group was laid down solely in mesodermal tissue, smooth and striated muscle, connective tissue and lymph nodes.

In recent years, two additional classes have been recognized: 1) the type occurring in conjunction with multiple myeloma; and 2) a primary type of amyloid occurring chiefly in the eye, larynx and urinary tract, as localized depositions or amyloid tumors. The latter, however, is really a misnomer as it is not a neoplasm. Shonhof rather preferred to call the nodule a "tumeroid amyloidosis." Primary amyloidosis of the bladder was first reported by Solomin in 1879, in a 73 year old woman in whom he found a plaque 8 cm. in diameter. Lucksch in 1904 found at post-mortem several small amyloid tumors in the bladder of a patient dying of pulmonary and intestinal tuberculosis. Chwalla in 1932 in Vienna described a tumor at the bladder neck which had been treated as a papilloma with fulguration repeatedly. Eventually, a suprapubic excision was accomplished and, although postoperative hemorrhage was troublesome, the patient recovered satisfactorily. The peculiar nature and staining reactions of this tissue were then discovered. In 1941 Rusche and Bacon reported 2 cases, one of which was treated by resection of the bladder effecting a cure, and the other by transurethral fulguration. Four years later there still remained amyloid tissue necessitating resection and fulguration transurethrally. Since then Corbitt, Broders and Pool of the Mayo Clinic, Purcell in 1946, and Craig in 1949, have described clinical cases. This is a total of 8 reported cases, two of which came from Europe 50 years ago.

All the etiological factors in amyloid disease are not understood but many of the theories have sound basis for argument. Eklund and Reimann reviewed several of these: 1) a general protein disturbance, 2) an antigen-antibody reaction, 3) an absorption of protein, 4) abnormality of the recticulo-endothelial system, and 5) hyperglobinemia. The nature of amyloid has been found to be a a compound consisting of protein and chondroitin sulphuric-acid, first pointed out by Friedreich and Kekule in 1859. Chwalla believed that the common cause for both generalized and localized amyloid to be in an abnormal course of destruction of cells, especially of nuclei. The protein thus destroyed was deposited as amyloid. Giving weight to this view is the high incidence of amyloid disease in a suppurative process and its resulting protein destruction. Experimentally, it has been shown that the injection of bacteria or chemical agents such as casein

into mice may produce extensive amyloid disease in the liver and spleen. Wichman felt that the process of deposition resembled infiltration more than it did disintegration or degeneration. At any rate, it seems reasonable to believe that there is at least some alteration in protein metabolism especially in the primary types, to initiate the process of tissue infiltration. The influence of diet on this process is interesting to speculate.

The diagnosis is entirely dependent on an able pathologist who, upon viewing the marked reduction in cellularity of the tissue, would seek special staining reactions. Characteristically, amyloid is stained by Congo red, crystal violet and iodine but, also, hemotoxylin and eosin, Mallory's connective tissue, and Van Giesen's stain are used. Cystoscopically, the tumor is strikingly similar to an infiltrating carcinoma of the bladder and will always be treated as such unless a preoperative biopsy is taken. The tumor usually appears as an irregular, localized, sessile, slightly elevated, reddish-yellow, ulcerated, hemorrhagic area. There may be multiple nodules of tumor tissue present instead or one circumscribed lesion.

The treatment, judging from the results of the clinical cases to date, consists of complete excision of the tumor, where possible, by suprapubic resection of the bladder. Transurethral resection and fulguration may not effect a cure but if carefully watched, may maintain the patient asymptomatic. Apparently the only serious complication, from the tumor itself, is recurrent hemorrhage. The growth of the tumor is assumedly progressive and, although the disease is not fatal, bleeding may reach very serious proportions from a large ulcerating spongy mass of amyloid. The effects of radiation, although unknown, may hold some promise of cure because of the protein nature of amyloid. Radon seeds were used in one case and the final results from its effects should prove very interesting.

CASE REPORT

A 49 year old white secretary entered the hospital on January 20, 1949, with a complaint of hematuria. Her first attack had been noticed 6 months previously, which had been completely painless and had cleared spontaneously in 24 hours. Eight days previous to admission, she had a recurrence of the hematuria which persisted 4 days, and then she sought medical advice. During this time she had been having frequency every 2 hours and nocturia 3 times, but no pyuria or dysuria. She gave no history of any previous illnesses with the exception of childhood diseases. She had had no weight loss.

The patient was a healthy appearing woman. The blood pressure was 155/80 and pulse 90. There was a mild conjunctivitis; the pupils reacted to light and accommodation. The nose and throat were clear. The lungs were normal, the heart was enlarged to the left but no murmurs were heard. The abdomen was soft without palpable organs. Extremities were normal.

On pelvic examination a rather firm, irregular mass was felt just anterior to the cervix, presumed to be in the bladder. The adenexae and uterus were normal.

Cystoscopy and intravenous urography were done. On the floor and posterior wall of the bladder was seen a large, flat, irregular, circumscribed, reddish mass

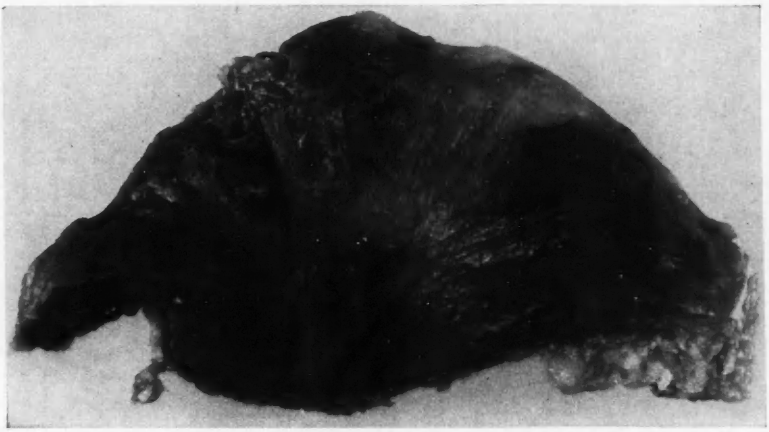

FIG. 1. Hemisection of resected portion of bladder, through lesion, showing small rim of relatively normal bladder.

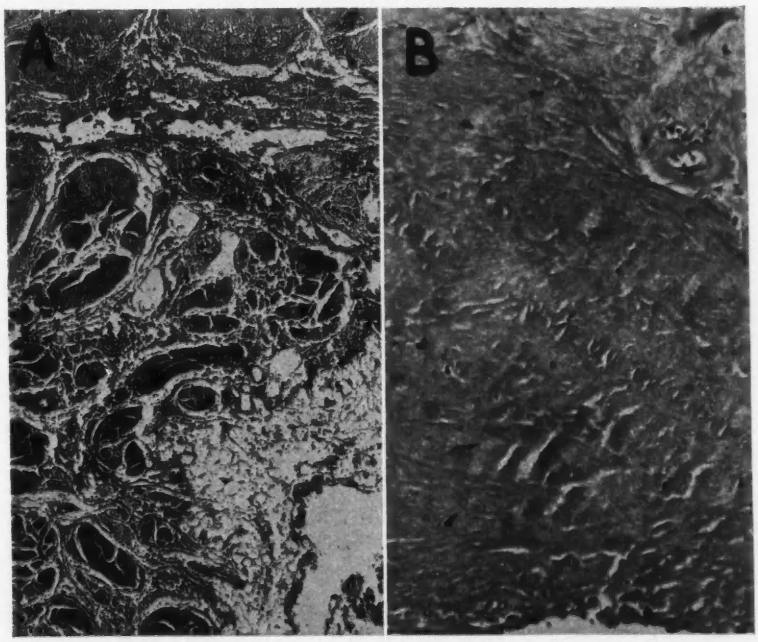

FIG. 2. *A*, low power view of relatively normal muscle bundles and diffuse deposit of amyloid adjacent. (× 15) *B*, Muscular coat, showing relatively diffuse hyaline deposit. (× 100)

6 by 8 cm. which appeared to be an infiltrating neoplasm. The mass extended down to, but did not involve, either ureteral orifice. The surface was ulcerated and bled easily. The decision was made to attempt a segmental resection of the bladder. Under spinal anesthesia, three-fourths of the tumor and about one-third of the bladder were removed. In the remaining portion of the tumor, ten radon seeds of 2 millicurie units each were implanted at 1 cm. distance apart. Postoperatively, the patient progressed well, and the wound healed spontaneously in 3 weeks. Aside from some frequency and tenesmus, she has had no difficulty since. Cystoscopy 3 months postoperatively disclosed no evidence of any remaining tumor formation, but the bladder capacity was limited to about 3 ounces.

Pathological report: Grossly, the resected portion of bladder (fig. 1) was abruptly but irregularly thickened except for the rim of the specimen by a circumscribed, apparently unencapsulated, firm, dull, brown and yellow mass measuring 6 by 5 by 0.8 cm. marked on the mucosal surface by numerous small pitted areas. On section, the cut surface presented a coarsely fasciculated, homogeneous, firm, hyaline-like, brown, yellow and gray appearance.

Microscopically, the smooth muscle cells and the fibrous connective tissue were markedly compressed and widely separated by a diffuse hyaline material (fig. 2). This material was rarely encountered in the arteriolar walls. It stained pink with Congo red and reddish violet with crystal violet; it gave a slate-blue color with Mallory's aniline blue connective tissue stain. The mucosa of the bladder was extensively denuded while the congested and edematous submucosa presented relatively intense, diffuse infiltration by endothelial leukocytes, lymphoid cells and eosinophils.

CONCLUSIONS

We have presented a discussion of primary amyloid disease of the bladder, with a report of 1 case.

Amyloid deposition is apparently on an alteration in protein metabolism basis.

Amyloid disease in the bladder is clinically undistinguishable from a carcinoma.

Treatment consists essentially of complete excision by the suprapubic or transurethral routes.

We wish to thank Dr. Ward H. Cook, Director of Laboratories, Long Island College Hospital, for assistance rendered in preparation of this report.

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PARARENAL TERATOMA: CASE REPORT

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Teratomas in and immediately adjacent to the kidney are seldom seen. The most recent case report that we have been able to find in the literature is that reported by Campbell in an infant 6 months of age. Nicholson has also reported a teratoma involving the kidney. Göbells lists 4 cases under the term of retroperitoneal teratomas. He makes no mention of the relationship of the retroperitoneal tumors with that of the kidney, except in one instance. He summarizes Hosmer's case of an 8 month old female infant. In this case the inferior surface of the teratomatous mass rested upon but was not adherent to the anterior surface of the kidney. The list of five retroperitoneal dermoid cysts, which is summarized by Göbells, contains only one instance, reported by Zwiefel of a tumor which was adherent to the kidney. It is apparent, therefore, that if one were more critical, the number of renal or pararenal teratomas are really few in number. The infrequency of pararenal teratomata, and the complicated clinical course of our patient have prompted us to make this report.

CASE REPORT

M. L., a 10 year old Negress, was admitted to the Cook County Hospital on January 1, 1946, with an admission diagnosis of an abdominal tuberculous mass and splenomegaly.

The patient's mother stated that the patient, who was markedly undernourished, had complained of intermittent pain in the left side of the abdomen near the left anterior costal margin ever since she fell and fractured 2 ribs 8 years ago. The pain episodes have been associated with bouts of fever. The patient had been under the care of a private physician, who suggested that her pain was possibly due to an old injury. The municipal tuberculosis survey of the housing project where the patient lived 1 year ago showed the entire family to be negative for tuberculosis. About 1 week ago, the child complained bitterly about the pain and screamed incessantly because of the pain which subsequently led to her hospitalization. There was no history of urinary difficulties. The patient had been constipated and had been treated for the latter condition by her mother with home remedies. The past history revealed the patient to have had pertussis, measles, and varicella. The family history was essentially negative. The father suffered from gall stones. The mother and brother were well. A sister had been in a hospital with diabetes mellitus.

Physical examination revealed a well developed, poorly nourished child who was not acutely ill but complained of pain in the left side. The blood pressure was 114 systolic and 60 diastolic. The head and neck were essentially normal. The

lungs were clear and resonant. The heart was of normal size and a soft apical and systolic murmur was heard. The abdomen was soft on palpation. The liver was not felt. Tenderness was elicited in the left upper quadrant. A firm, nodular deep lying mass was palpated near the flank and under the left costal margin.

The genital organs were normal. The neurological examination afforded normal findings. The laboratory findings were as follows. Blood Wasserman reaction was negative. Culture for Klebs-Loeffler bacillus was negative. Vaginal smear was negative for gonococci. The blood hemoglobin was 72 per cent. The red blood cell count was 3,870,000 per cubic millimeter. The color index was .96. The white blood cell count was 11,600 per cubic millimeter with a predominance of polymorphonuclear leukocytes. The blood platelet count was 307,000 per cubic millimeter. The blood was negative for active or latent sickling.

Blood chemistry values were normal. There was a total protein of 6.8 gm. per 100 cc and a blood calcium of 9.5 mg. per 100 cc. The blood diastase on a fresh blood sample was 32. The Mantoux test was 2 plus.

The initial x-rays revealed the heart and lungs to be within normal limits. A flat film of the abdomen revealed a circular area of calcification superimposed over the superior pole of the left kidney in the region of the tenth, eleventh, and twelfth ribs. This finding was interpreted as possible calcification within the spleen, kidney or adrenal gland. Lateral films were taken only to add additional possible x-ray diagnoses such as calcified hematoma following old fracture of ribs, or possibly a Wilms' tumor of the kidney or a calcified hematoma of the kidney.

Intravenous pyelograms were obtained on January 16, 1946. A preliminary film showed a mass in the left upper abdomen which was mottled by areas of calcification. The injection of the dye visualized the right kidney, pelvis, calyces, ureter and bladder very well. They were normal in appearance. The calyces of the left kidney were obscured by the calcified mass; however, the left ureter was well visualized in the 5 minute film. The lateral view showed the mass to be anterior to the kidney. This fact indicated that the mass might be part of the kidney structure.

Roentgen studies of the skull were normal. Roentgen studies of the gastrointestinal tract were normal, except for a defect in the left posterior lateral wall of the descending colon due to extrinsic pressure by the calcified mass. There was also a slight depression of the distal end of the transverse colon which was most likely due to extrinsic pressure by the calcified mass.

An abdominal exploratory operation was performed on January 31, 1946. A retroperitoneal calcified tumor mass about the size of an orange was found. The mass was under the base of the transverse mesocolon and against the upper pole of the left kidney. It was movable up and down but less movable by lateral or medial traction. The pancreas was located on the upper margin of this mass but was not involved by the tumor mass. The surface was grayish white in color with a few dilated veins over the surface and at the time was thought to resemble a sarcoma. The mass was considered inoperable. A biopsy was taken and about an ounce of a purulent like material was removed for culture. The capsule of the mass was sutured and the abdomen was closed.

Microscopic examination of the retroperitoneal cyst wall revealed that the wall was composed of a dense fibrous connective tissue which contained small focal accumulations of lymphocytes. These findings were considered diagnostic of a nondescript cyst wall of the retroperitoneal space.

Cultures for tubercle bacilli and other organisms in aerobic and anaerobic media were negative. A direct smear, however, was reported to show many acid fast organisms. This latter finding delayed the proper treatment which was subsequently carried out. Routine laboratory studies were repeated and were all essentially normal.

The patient was discharged from the hospital on March 18, 1946, 74 days after the first admission to the hospital without any decided improvement.

The patient was readmitted August 27, 1948, two years and 5 months after her previous dismissal from the hospital. Her present complaints were that 30 days after surgery she experienced attacks of dysuria, frequency, urgency and difficulty in starting or stopping the urinary stream. Hematuria was noted on one occasion about 3 months after her first operation. The pain in the left upper quadrant became quite severe whenever the patient was moved.

The physical findings were essentially the same as they were on her first admission to the hospital except for the above mentioned urinary symptoms and a slight daily rise in temperature. The laboratory examination of the urine was negative for blood, sugar, albumin, and acetone. The blood hemoglobin was 57 per cent. The stomach washings were negative for the bacillus of tuberculosis.

The clinical diagnoses considered at this time were tuberculosis of the left kidney, left ureteral stricture, and Pott's disease with an associated tuberculous abscess.

Her urinary symptoms prompted a more concentrated study of the urinary tract.

On September 14, 1948 a 16 F cystoscope was passed with ease. The bladder urine was crystal clear. The bladder had a good capacity and tonus. There was evidence of a trigonitis and inflammatory hypertrophic tissue on the inferior rim of the vesical neck. The rest of the mucosa of the urinary bladder was grossly normal. Both ureteral orifices were clearly seen and the efflux from both ureters was clear. Both ureters were catheterized with 4 F catheters with ease. No obstruction was noted. Intravenous phenolsulfonphthalein was secreted from the right kidney in 5 minutes in excellent concentration and in 10 minutes from the left kidney in good concentration.

Urine examination for tubercle bacilli was negative.

Bilateral retrograde pyelography was done. The large calcified density, which had been seen in the left upper quadrant in the preliminary film, had a mottled placque-like configuration and a rather sharp delineation of its margins (fig. 1, *A*). Catheters were present in both ureters. The upper pole of the left kidney and the catheter were superimposed on the oval calcific density (fig. 1, *B*). The left pyelogram seemed to occupy a position over the calcified mass (fig. 1, *C*). The superior and inferior minor calyces were normal. The middle calyx was not visualized with any degree of certainty. The ureter on the left side showed a slight

spiral configuration but did not have the appearance of a tuberculous ureter. The right pyelogram was interpreted as normal. A lateral view of the left pyelogram

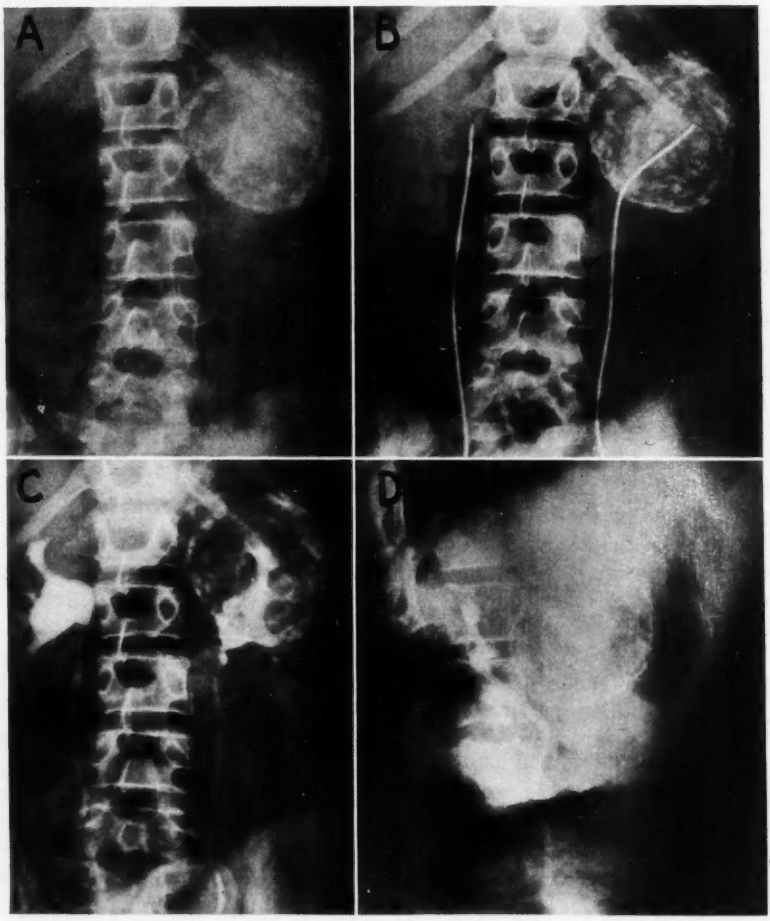

FIG. 1. *A*, preliminary roentgen study to show large calcified density in left upper abdominal quadrant. *B*, left ureteral catheter seems to be superimposed on oval calcific density. *C*, left pyelogram seems to occupy a position over calcified mass. Middle calyx was not visualized with certainty. *D*, lateral view of left pyelogram, revealing that circular calcific mass is anterior to kidney.

showed that the circular calcific mass was just anterior to the renal collecting system (fig. 1, *D*). It seemed to push the left kidney posteriorly and produced some angulation of the catheter on the upper portion of the left ureter and some

rotation of the calyces and pelvis of the kidney. The position of the mass was considered as retroperitoneal and anterior to but bound to the anterior surface of the kidney near the hilus.

Consultation with the pediatric staff by one of us (W. J. B.) led to a final decision to remove the calcific mass through an extraperitoneal lumbar incision.

The patient was operated upon October 2, 1948, through a left lumbar incision. The retroperitoneal mass was mobilized with a moderate amount of difficulty and it was found to be intimately adherent to the renal pedicle and anterior surface of the left kidney. It was found necessary to remove the left kidney with the mass since it was impossible to separate the mass from the kidney even by sharp dissection.

The patient made an uneventful recovery and was discharged from the hospital on the twelfth postoperative day.

One month later the patient was re-admitted for a draining sinus which was treated for 17 days. The patient again was discharged much improved and with a 5 pound gain in weight.

The specimen, submitted to the department of surgical pathology, consisted of a left kidney measuring 10 by 3.5 by 4.0 cm. The capsule stripped with ease. The surface was smooth, light purplish tan gray in color and presented distinct fetal lobulations. On sectioning, the cortex of the kidney was up to 4 mm. in thickness and of a pale purplish tan-gray color. The medulla of the kidney was a slightly darker purple gray. The calyces were slightly dilated and the pelvis of the kidney was slightly compressed. The mucosa of the pelvis was edematous, light gray in color, and mottled by small pin point sized submucous hemorrhages. There was a large calcified mass measuring 8.0 by 4.5 by 5.5 cm. which was firmly attached to the hilus of the kidney, anterior to the pelvis and ureteropelvic junction (fig. 2, *A* and *B*). The surface of the mass was covered by thick, adherent, fibrous tags which were reddish gray in color and granular. On sectioning the mass, a partially cystic structure was exposed (fig. 2, *B*) and this was filled with a necrotic, calcareous, pasty material which was light yellowish gray in color. The wall of the cyst was up to one centimeter in thickness. The upper pole of the cyst was filled by a polypoid mass which was reddish gray in color and distinctly lobulated (fig. 2, *B*). On sectioning through the polypoid tumor mass the cut surface was light yellow to grayish white in color and was covered with a reddish gray granular membrane.

Microscopic sections of the kidney, of the wall of the calcified mass, and of the polypoid tumor mass within the cystic cavities were made and stained with hemalum and eosin.

Section of the kidney revealed a moderate congestion of the glomeruli and coagulated protein material in some of the dilated convoluted tubuli and in Bowman's spaces.

A section of the thick cyst wall revealed a nondescript wall formed by dense fibrous connective tissue impregnated with calcific material and infiltrated by small numbers of lymphocytes. In places, the wall contained small needle shaped

clefts (cholesterol clefts) surrounded by partially calcified cellular-like structures. In some places, the lymphoid accumulations surrounded thin wall blood vessels, while in others, they surrounded small bundles of myelinated nerve fibers.

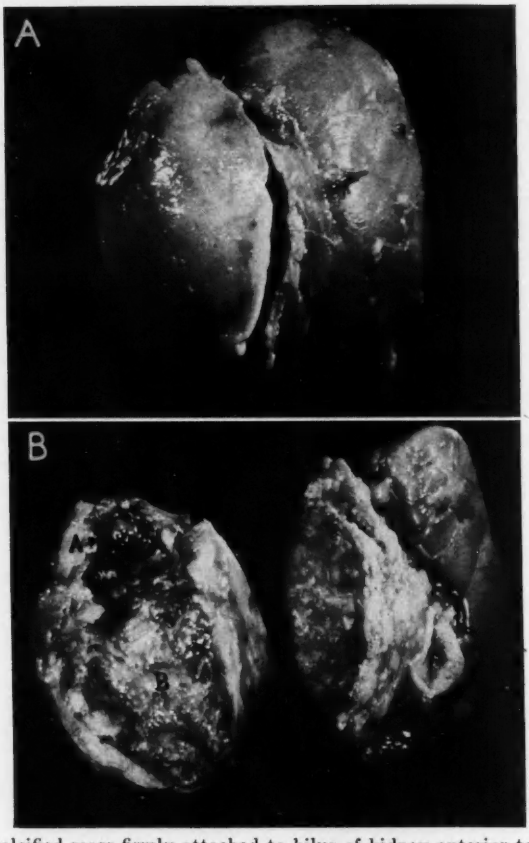

FIG. 2. *A*, calcified mass firmly attached to hilus of kidney anterior to pelvis and ureteropelvic junction. *B*, cystic cavity filled by necrotic calcareous material, *B*, and a polypoid mass in upper pole of cyst, *A*.

A section of the wall of the cyst which was adherent to the kidney showed a definite line of demarcation between the renal parenchyma and the cystic tumor mass (fig. 3, *A*). The capsule of the kidney in this area seemed to be incorporated with the wall of the calcified mass, and the wall in this area showed focal accumulations of round cells, bundles of smooth muscle fibers which were embedded in loose connective tissue, and nests of dilated blood vessels.

Section of the polypoid mass, which protruded into the gruminous calcareous material of the cystic portion of the tumor, revealed variegated cellular struc-

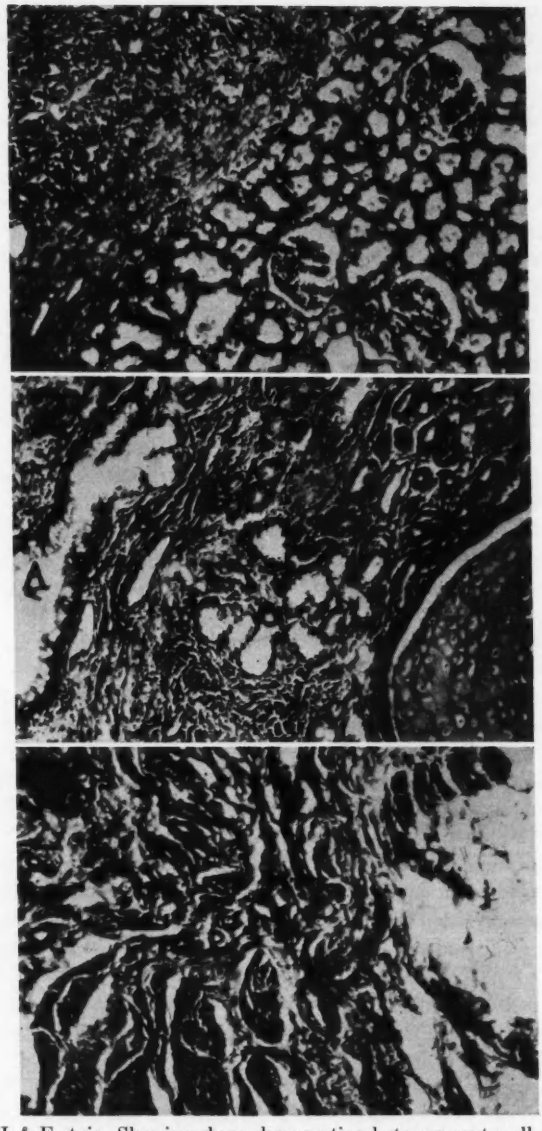

FIG. 3. *1*, H & E stain. Showing sharp demarcation between cyst wall and renal parenchyma. Note small dilated blood vessels and foci of lymphocytes in wall of cyst. *2*, H & E stain. Showing ciliated columnar epithelial cells (resembling bronchial mucosa) at *A*; bundles of smooth muscle at *B*; mucus secreting glands at *C*; serous secreting glands at *D*; and mature hyaline cartilage at *E*. *3*, H & E stain. Showing bundles of smooth muscle fibers, vascular fibrous connective tissue and fat tissue.

tures. In places the tissue was suggestive of bronchial mucosa as characterized by stratified ciliated columnar epithelium (fig. 3, *B*), covering nests of mature hyaline cartilage (fig. 3, *B*), bundles of smooth muscle fibers, and mucinous and serous glands (fig. 3, *B*). In other areas there were nests of small acinar structures whose cells showed a finely granular reddish staining cytoplasm resembling serous secreting salivary gland-like structures. Still other places revealed large acini whose cells showed a pale pink staining cytoplasm suggestive of convuluted tubuli of the renal cortex. However, this latter finding is most difficult to prove in the absence of glomeruli, glomerular-like structures or collecting tubules. Fat, smooth muscle fibers (fig. 3, *C*), foci of lymphocytic proliferations and myelinated nerve fibers were also seen.

DISCUSSION

It is apparent from our findings that we are dealing with an unusual tumor mass which is markedly adherent to the kidney and can be rightfully considered a pararenal teratoma. The number of pararenal teratomas would be augmented if we included the so-called dermoid cyst, which in reality is a teratoma. That the dermoid is a teratoma or form of a teratoma is supported by the comments of Novak, who states that it is evident that no sharp dividing line can be drawn between the dermoid and teratoma since, in the former, which is characterized by a predominance of ectodermal elements, mesodermal and occasionally tissue from the endodermal layers are also found. Furthermore, the histogenesis of the two is identical.

Willis objects to the term dermoid cysts for two reasons. Firstly, that the same name, dermoid cysts, is applied to lesions unrelated to teratoma such as sequestration dermoid cysts of the skin, cranial cavity, and other parts; secondly, to call teratomas dermoid cysts is to give always an incomplete and often erroneous idea of their structure. Frequently a predominating skin lined cyst is found in teratomas. In such instances careful examination of the wall of the cyst reveals a nub of tissue containing tissues other than skin. This has been a frequent finding in our laboratory experience.

On the basis of the above support we do not hesitate to include the dermoid cysts of the kidney that are reported in the literature, being careful to exclude those cystic tumors which have been described by Valentine and by Ross where definite histological findings are lacking for the diagnosis of dermoid cysts or teratomas.

Of the cases summarized by Göbell, Ross, Walker, Baldwin, and presented by Campbell, Nicholson and the case we report here, a total of 15 cases have been described in the world literature

As to pathogenesis a number of theories have been presented. The blastomere theory of Marchand Bonnet and the sex cell theory of spontaneous growth of the unfertilized ovum, are purely speculative according to Novak.

Although we do not propose any theory as to the pathogenesis, we are inclined to agree with Willis that one must look to the experimental and chemical embryologist for the final solution of the growths of teratomas. They may be entirely

benign. A small percentage of them may undergo malignancy. It is emphasized by Willis that teratomas are tumors arising from foci of plastic pleuropotential embryonic tissue which escaped from the influence of the primary organizers during early embryonic development. This escape is in some way related to disturbances which emanate from the invaginated organizing tissues of the primitive streak and affect median or paramedian parts in close relationship to these tissues. As a result the affected primordium, as it grows, differentiates in accordance with its own "labile determinations" producing a variety of tissues foreign to the part in which it grows. If these tissues differentiate and mature as fast as they grow, a benign cystic teratoma results. If the tissues fail to mature completely but retain their capacity for continued growth at the embryonic level a malignant, embryonic teratoma results.

SUMMARY

A pararenal teratoma with the clinical and pathological pictures has been presented. The pathogenesis of these tumors has been reviewed.

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CONCOMITANT BILATERAL MALIGNANT TESTICULAR TUMORS

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Co-existent cancer of both testes is remarkably rare. The Tumor Registry of the Army Institute of Pathology at Washington, D. C. has over seventeen hundred case records of testicular tumors in the files without a report of simultaneous bilateral malignancy in fully descended testes. A review of the medical literature to the year 1805 yielded 21 records of men having normally located testes with proven cancer present in each. Most of the tumors developed simultaneously, although a number of the men observed enlargement of one testis several months before the other became affected. Hamilton and Gilbert's exhaustive analysis of 7,000 case records of testicular tumors resulted in the collection of 134 cases where each testis was involved with cancer at some time. Usually months, or more often, years elapsed between the removal of a unilateral tumor and the involvement of the second testis. They were impressed with the strong propensity for carcinogenic development in the remaining testis and reached the conclusion that this tendency was several hundred times greater than chance association. Ectopia of the testes significantly increased the risk of bilateral malignancy.

The accompanying summation of the 21 reported cases of concomitant bilateral testicular cancer in scrotal testes (table 1) presents three distinctive features. There is a relatively large proportion of lymphoid tumors, the survival rate is extremely low and the average age incidence is 51 years in contrast to 35 to 39 years for unilateral tumors.

ABSTRACT OF CASE HISTORY

P. P., a white man aged 67, was admitted to Bellevue Hospital May 11, 1948; he died October 29, 1948. His chief complaints were enlargement of both testes and ulcers of the face. The past history revealed a fracture of the right tibia and fibula, 1934; ulcers of the right leg had been present since. One year ago the patient noticed painless enlargement of the left testicle, followed by enlargement of the right testicle 3 months later. Six months ago he observed an ulcer over the left parotid region of the face, followed by development of about ten similar lesions of the face and forehead. See figure 1, *A*.

The temperature was 98 F, pulse 84, respirations 20, blood pressure 132/86. The patient was well developed and well nourished. Scattered over the face were ten round nodules averaging 0.5 by 3.5 cm. They protruded above the surface of the skin; some had intact epithelium, others, ulcerated craters (fig. 1, *A*). They were firm and pink in color. On the right leg and foot were several ulcers 10 cm. in diameter. There was considerable bony deformity and some edema of the right leg and foot. The scrotum was enlarged five times normal size. Both testes were enlarged to about 10 by 7 cm., were painless, and filled the scrotum to the external inguinal ring. The surface was smooth and no light was trans-

TABLE 1. *Summary of cases to date*

REFERENCE	AGE	PATHOLOGICAL DIAGNOSIS, RIGHT AND LEFT TESTES	COMMENTS
Bidard 1853	27	Encephaloid cancer	Right enlarged slowly over 2 year period. Left enlarged previous 5 months. Right removed. Died 3 months. Autopsy.
De Launay 1860	30	Encephaloid	5 months duration on left. Right found enlarged on examination. Died 6 months. Autopsy.
Silbey & Hulke 1866	57	Scirrhus cell	Right testicle enlarged for 12 months. Left for 9 months prior to removal of both.
Murphy 1885	74	Spindle cell carcinoma	Right testicle enlarged followed in few weeks by left. Bilateral orchidectomy. Again quoted by Kober in summary 144 cases.
Loeper & Louste 1904	34	Lymphadenoma	Also quoted by Chavassu (1906). #128 Autopsy. Multiple tumors in trachea and bronchi.
Kaufman 1907	30	Interstitial cell tumor	No clinical history.
Kaiser 1920	55	Small round cell sarcoma	Bilateral tumor 2 months duration. Bilateral orchidectomy. Extensive metastasis 5 months later.
Tanner 1923	45	Carcinomatous teratoma	Right testicle enlarged 6 months followed in 3 months by left. Bilateral orchiectomy. Died 4 months.
Higgins 1928	54	Embryoma	Bilateral orchiectomy. Left testicle enlarged more than a year. Right found enlarged at operation. Died 1 year later.
Dew 1928	84	Lymphosarcoma	Right side scrotum enlarged some weeks. Slight enlargement left testicle on examination. Cutaneous metastases. Died. Limited autopsy.
Aloi 1929	60	Spindle cell sarcoma	Bilateral tumor 5 months duration. Bilateral orchiectomy. No notes on outcome.
Wollheim 1930	66	Lymphosarcoma	Bilateral enlargement 6 weeks duration. Died 6 months following bilateral orchiectomy.
Colby 1930	62	Lymphosarcoma	Tumor nasopharynx removed 8 months prior to bilateral enlargement testes 5 weeks before orchiectomy.
Sicard & Pavie 1930	54	Lymphocytoma	Overnight bilateral testicular enlargement Inoperable. Died 1 month. Autopsy—diffuse metastases.
Venable & Flynt 1931		Embryonal carcinoma	Right testicle enlargement slowly over period 5 years. Left testicle enlarged 1 year prior to bilateral orchiectomy.
Pierson 1932	38	Embryonal carcinoma	Left testicle enlarged 2 months. Right found enlarged on examination. Orchiectomy. Living 3 years after operation.
Townsend 1935	51	Lymphadenoma	Admitted to hospital with bilateral testicular tumor and abdominal mass 5 weeks duration. Died 2 weeks. Autopsy.

TABLE 1.—*Continued*

REFERENCE	AGE	PATHOLOGICAL DIAGNOSIS, RIGHT AND LEFT TESTES	COMMENTS
Lewis & Priestley 1938	44	Adenocarcinoma	Painless enlargement both testes for 2 months. Bilateral orchiectomy. Extensive metastases within 3 months.
Graves & Lawrence 1942	33	Embryonal	Right testicle enlarged 2½ years followed 1 year later by left. Bilateral orchiectomy. No recurrence 10 months later.
Smith 1943		Embryonal carcinoma	Clinical course not stated. Bilateral orchiectomy.
Gill & Howell 1948	73	Embryonal cell carcinoma	Right testis enlarged 1 year ago. Left 3 weeks prior to examination. Bilateral orchiectomy.

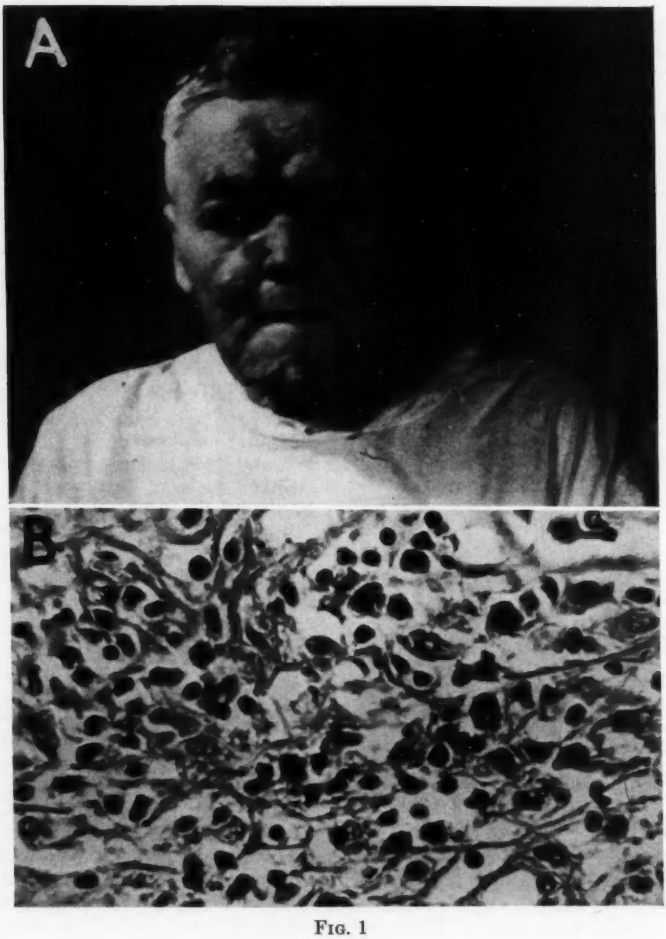

FIG. 1

mitted through the scrotum. There was no palpable enlargement of the lymph nodes, nor was there any detectable enlargement of the liver, spleen or other viscera. Except for generalized arteriosclerosis, there were no other significant findings.

Blood studies: Red blood cells, 3,500,000; hemoglobin, 12.5 gm.; white blood cells, 9,200. Differential: Polymorphonuclears, 67 per cent; lymphoctes, 21 per cent; monocytes, 2 per cent; eosinophiles 7 per cent; basophiles 3 per cent. Urine: normal. Mazzini: Negative. Stool: Negative for blood.

Blood chemistry: Nonprotein nitrogen, 35 mg. per cent; chlorides, 580 mg./L.; cholesterol, 224 mg. per cent; sugar, 105 mg. per cent; cephaline flocculation, negative; icterus index, 6 units; albumin, 4.3 gm./L; globulin, 2.6 gm./L; acid phosphatase, 1.0 units; alkaline phosphatase, 3.7 units; vitamin C, 0.2 mg./100 cc. Aschheim-Zondek test: Negative.

X-ray reports in abstract: Heart, lungs and aorta normal. Gastro-intestinal series normal. Bone x-rays of skull and spine normal. Kidneys, ureters and bladder showed no evidence of disease.

The patient was examined by consultants from departments of dermatology, otolaryngology, radiation therapy and hematology. No lesions of the nasopharynx were found. The skin lesions of the face were biopsied and on August 17, 1948, a bilateral orchiectomy was performed. Convalescence was uneventful.

Pathological report of testes: Acc. No. 3255–48. Clinical diagnoses: Carcinoma of testes. Source of specimen: Testes. Specimen received in Bouin's solution consisted of 2 large masses of tissue, the larger of which measured 15 by 2 by 8 cm., the smaller 12 by 8 by 9 cm. The tissue was rubbery in consistency with a smooth external surface. On cross section one of the masses showed a soft, light brown, friable mass of tissue. At one pole there was pale yellow firm material, and just above this, a remnant of the epididymis could be seen. The other specimen cut with moderate resistance and on cross section a similar pattern was demonstrable.

Microscopic examination of several sections of both testicles revealed an extensive malignant tumor which had all but effaced every remnant of normal testicular tissue. In a few places there were isolated epididymal glands and vestiges of the tunica albuginea, tunica vaginalis and spermatic cord. No seminiferous tubules were identified. The tumor was characterized by growth of large masses of undifferentiated cells with few identifying characteristics. These cells showed a moderate degree of pleomorphism, particularly in shape and staining characteristics. Only scanty stroma had been elaborated so that thin fibrils separated small clusters of cells from each other; however, there was no distinctive pattern. Large portions of the growth had become necrotic and much hematoid had been deposited in these areas. The growth was poorly vascularized.

The predominant cell type had a nucleus about twice the size of a small lymphocyte and this was rather heavily stained but vesicular. These nuclei were round oval or slightly indented. Only a few were in mitosis. They resembled the immature cells seen in the germinal centers of lymphoid follicles.

They had almost no distinguishable cytoplasm and no distinct cell membrane. The growth differed from the usual carcinoma and embryonal carcinoma of the

testes in that it was bilateral, because it lacked both alveolar and papillary structures, pseudotubercles, lipid rich cytoplasm and because the usual double cell type with the small lymphocytic cell types interspersed between large vesicular nuclei were not observed. The tumor cells here were considerably smaller and less vesicular than the characteristic cell of the seminoma. Furthermore no teratomatous elements were discovered. Diagnosis: Reticulum cell sarcoma (fig. 1. *B*). Dr. S. F. Wilens.

Pathological report of skin lesion: Skin biopsy was reported as reticulum cell sarcoma.

External radiation (400 r) of the facial lesions resulted in initial slight improvement but were discontinued because of inadequate response. A course of nitrogen mustard was given without noticeable effect. The leg ulcers became necrotic. Arterial pulsation was not discernible. An amputation of the right leg was performed on August 16, 1948. Rapid deterioration followed. On October 21, 1948, the right inguinal lymph nodes were found to be enlarged but, because of the terminal state of the patient, a biopsy was not performed. Death occurred on October 29, 1948, 170 days after admission. No autopsy was obtained.

DISCUSSION

It would be imprudent to assume that this report is the only record of bilateral reticulum cell sarcoma of the testes. The confusion of nomenclature was discussed by Chevassu in 1906, when he arrived at the conclusion that many cases of lymphosarcoma were, in reality, varieties of seminomas. He called attention to a class of tumors reported in the French literature as lymphadenoma which were ultimately bilateral, had a rapid course, often had cutaneous growths, and had histological structures resembling lymphosarcoma. Dew in 1928 emphasized the difficulty, if not impossibility, of identifying the primary lesion. He was inclined to believe that the testicular and cutaneous lesions were all a part of a "general lymphocytic deposit." Bilateral enlargement of one or both testes with leukemic infiltration has been observed in acute leukemia and in Hodgkin's disease.

Consequently, we infer that reticulum cell sarcoma of the testes has appeared under a variety of terminologies, which fact prohibits a true appraisal of the actual incidence. Our patient first noticed enlargement of the testes as the initial sign of his disease. We do not assume, however, that the primary lesion was in the testes, but prefer to regard reticulum cell sarcoma as a generalized neoplasm of the reticular system. The combination of lymphosarcoma of skin and testes has been recorded several times since first described by Malassez in 1877. The co-incidence of nodular and ulcerated skin lesions and enlargement of the testes is perhaps the most helpful diagnostic aid in suspecting a lymphoid tumor of the testes.

The words of Willis are particularly appropriate to this subject, for there is great need for unanimity of thought on the character and classification of lymphoid tumors. He states: "Nowhere in pathology has a chaos of words so clouded clear concepts as in the subject of lymphoid tumors." He believes that the redun-

dant nomenclature results from an attempt to make unwarranted distinctions based on relative rates of growth of cells comprising the tumor. These various degrees of differentiation are almost infinite in number and variety, merging into one another without clear boundaries of demarcation. There has arisen thereby a formidable vocabulary for lymphoid tumors, particularly puzzling to the clinician, if not to the pathologist.

The kinship between the lymphoid tumors may be brought into focus by his simplifications, calling attention to the fact that the tumors have two essential components: lymphocytes and reticuloendothelial cells. Both of these arise from a common origin in the primitive mesenchyme developed early in embryonic life from the middle germ layer or mesoderm. The reticulum differentiates from the early connective tissue cells by branching into a syncytium. Nutrition to the connective tissue is supplied from the lymph, either by fine canals or by permeation, so that an intimate contact with the lymphoid system is established. The role of reticulum cells in the body economy is largely passive, serving as supportive tissue for binding and holding other tissues in place. Reticular connective tissue is fibrous in type and is found in many structures such as lymph glands, spleen, intestine, bone marrow, liver, skin, kidneys, lung, ovaries and testes.

The classification of lymphoid tumors by Willis follows. It is established on the premise that all tumors of lymphoid tissue are related variants of one disease:

1. Follicular lymphoma (least malignant).
   a) Localized benign lymphoma.
      Slow enlargement of a single gland.
   b) Multiple malignant form.
      Slow enlargement of one or more groups of glands with extension to other glands.
2. Lymphosarcoma with or without leukemia.
   Malignant tumor of the lymphoid tissue which is predominantly lymphocytic or lymphoblastic. The presence of malignant lymphocytes or lymphoblasts in the circulatory blood is merely circulating metastasis.
3. Hodgkin's disease.
   A form of sarcoma of lymphoid tissue showing differentiation of both lymphoid and reticulum elements with accompanying fibrosis.
4. Reticulum cell sarcoma.
   Closely allied structurally to Hodgkin's disease but has only (or predominantly) a differentiation of neoplastic cells toward reticular connective tissue. The tumor has fibrous tissue and polyhedral cells in various states of metastasis. Blood vessels and plasma cells are often seen and necrosis is common. Most of the tumors have occurred in the adult male and spread from gland to gland as well as by blood stream.

SUMMARY AND CONCLUSION

A review of the documented reports of co-existent bilateral tumors of the testes reveals that the carcinomatous neoplasms usually appear in one testis before the other becomes enlarged. Sarcomatous lesions are more truly simultaneous in their

development. The association of nodular or ulcerated lesions of the skin with tumor development in one or both testes constitutes a syndrome of clinical usefulness in establishing a preoperative diagnosis of a lymphoid tumor. The average age of men having bilateral sarcoma of the testes was 58 years in contrast to 47 years for those with bilateral carcinoma. All bilateral testes tumors have a bad prognosis. The sarcomatous lesions exhibit a particularly rapid course to death. A case report of bilateral reticulum cell sarcoma of the testes is reported herewith, together with a discussion of the classification of lymphoid tumors.

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RENAL APLASIA: TWO CASE REPORTS

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The aplastic kidney may be only a small mass of undifferentiated scar tissue.[1] Its identification is difficult and often is possible only upon histological examination. This small renal remnant is doubtless frequently overlooked and a mistaken diagnosis of true renal agenesis may be made in clinical and autopsy studies. Less frequently the aplastic kidney is large, cystic and easily palpable. When such a tumor mass exists in the loin[2] its probable relation to the urinary organs is readily recognized. However, its true nature more often will be disclosed only at operation. The records of 2 children who had the latter type of renal aplasia are the basis of this report.

CASE REPORTS

C. C. F., M. H. No. 11310, male, aged 16 months, was admitted to Methodist Hospital on July 31, 1942, because of a swelling in the left side of the abdomen, dysuria and fever. The father and mother were living and well. There were 2 sisters and 1 brother, aged 22, 19 and 17 years respectively, who were living and well. The family history was negative except that one grandmother had had pumonary tuberculosis and asthma. The child had had no previous serious illness. He was a well developed boy of stated age.

Examination of the head and chest was negative. There was a marked asymmetry of the abdomen due to a bulging of the upper left quadrant caused by a globular, smooth mass occupying the left renal fossa. This was movable, ballotable, not tender, and was elastic to touch (fig. 1). Neither the right kidney nor the bladder was palpable. The extremities and the external genitals were normal.

The abdominal swelling was discovered soon after birth, and had gradually increased in size. There were no symptoms due to its presence prior to the present illness. However, the child had a peculiar stature with a marked lordosis. A few weeks prior to his admission he had developed dysuria and for 2 weeks was febrile. When admitted his temperature was 103.8 F. The urine contained 90 to 100 pus cells per high power field in the centrifuged specimen. The hemoglobin was 45 per cent. Red blood count 2,120,000, white blood count 15,300, with 62 per cent polymorphonuclears and 38 per cent small lymphocytes. Nonprotein nitrogen was 20 mg. per cent. The phenolsulfonphthalein was 0 per cent the first hour, 9 per cent the second hour. The blood pressure was 100 systolic and 60 diastolic.

[1] Nicholson, G. W.: The kidneys and their development. Guy's Hosp. Reps., **77**: 362, 1927.

[2] Kraus, L. W. and Straus, R.: Retroperitoneal cyst arising in persistent metanephros with congenital absence of right kidney and ureter. J. Urol., **34**: 97, 1935.

On August 3, 1942, a cystoscopy failed because of an obstruction at the penoscrotal angle of the urethra. A cysto-urethrogram showed a small, irregular bladder shadow with a reflux on the left side. The left ureter extended almost to the crest of the ilium where it was bifurcated and terminated in blind endings (fig. 2, *A*). A soft rubber catheter was anchored in the bladder. Repeated blood transfusions, intravenous fluids, and urinary antiseptics were given. The child improved under this management and 1 week later, August 10, cystoscopy was performed. The prostatic urethra was large and contained four or five abnormal outlets on its floor. These cavities seemed to extend underneath the bladder base. The vesical orifice was slightly elevated and there was moderate trabeculation, and slight cystitis. A normal right ureteral orifice was easily located and catheterized without difficulty. The urine from the right kidney was infected. The right ureteropyelogram showed moderate dilation of the right pelvis and ureter. A left ureteral

FIG. 1. Case 1. Child on left shows protuberant abdomen due to aplastic cystic kidney mass.

orifice could not be located. There was some irregularity of the trigone due to a lack of full development of the left side. A ureteral catheter was passed into one of the cystic openings in the prostatic urethra and skiodan injected. This demonstrated a slight ureteral reflux on the left side (fig. 2, *B*). Catheters were anchored in the right ureter and the bladder. The child rapidly improved. On August 24 the phenolsulfonphthalein output was 24 per cent, and the temperature was 99 to 100 F. However, the parents became dissatisfied and removed the patient from the hospital without official release.

On September 12, 1942, one month after the boy was taken home, he was admitted to the James Whitcomb Riley Hospital For Children, No. 63050. His temperature was 99.5 F and the white blood count was 21,000. There was a moderate number of pus cells in the urine and the urine cultures showed B. coli. Repeated stains of the urine sediment for tubercle bacilli were negative. Frequency and dysuria became worse. The phenolsulfonphthalein output in 75 minutes was 3 per cent. The blood urea nitrogen was 13 mg. per cent and the nonprotein nitrogen was 28 mg. per cent at this admission. The physical examination was negative except for the palpable mass in the left upper abdomen.

On September 16, 1942, a flat x-ray film showed a large, opaque, spherical mass occupying the entire left side of the abdomen. It was of uniform density and extended from the left diaphragm to the crest of the left ilium, and crossed the midline medially. The colon and small bowel were displaced upward and to the right. The intravenous urogram showed a rather large right pyelogram with a normal pattern. The right ureter was moderately dilated and was slightly tortuous. There was good excretory function on the right side, but no dye was present on the left side. On September 18, 1942, cystoscopy again failed to disclose the presence of the left ureteral orifice. Attempts to visualize again the left ureter by injecting the prostatic cavities were failures. The cystogram was normal.

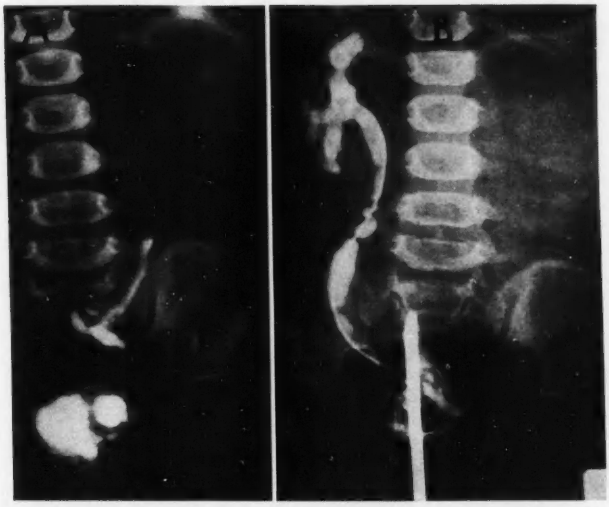

FIG. 2. Case 1. *A*, cysto-urethrogram, showing reflux up incomplete left ureter with bifid upper end. *B*, right pyelo-ureterogram shows dilation. Injection of opening in prostatic urethra visualizes lower left ureter.

A diagnosis of probable left renal tumor was made and x-ray therapy was instituted; 1200 r. u. renal tumor dose were given. This had no appreciable effect upon the size of the mass.

On October 24, 1942, the patient was operated upon. The preoperative diagnosis was obstruction of a bifid left ureter which opened in the posterior urethra, with destruction of the left kidney, probably by a non-radio-sensitive neoplasm.

Through a loin incision a post-peritoneal mass was exposed. It was firm, nodular, about 5 cm. long, of a dusty gray color, and had a wrinkled appearance on the surface. This was interpreted as a small nodular kidney. Upon attempting its removal it was found attached to a perfectly smooth, globular mass 9 or 10 cm. in diameter, which arose from its deeper surface. The entire structure was easily removed. At no time was a vascular pedicle or ureter found. The suprarenal gland

was normal in appearance. There was no other tissue suggesting a left kidney present in the left loin or the iliac basin. The cephalic terminations of the previously visualized left ureter were not found. The wound was closed with drainage. The postoperative course was normal, the child leaving the hospital 3 weeks after the operation.

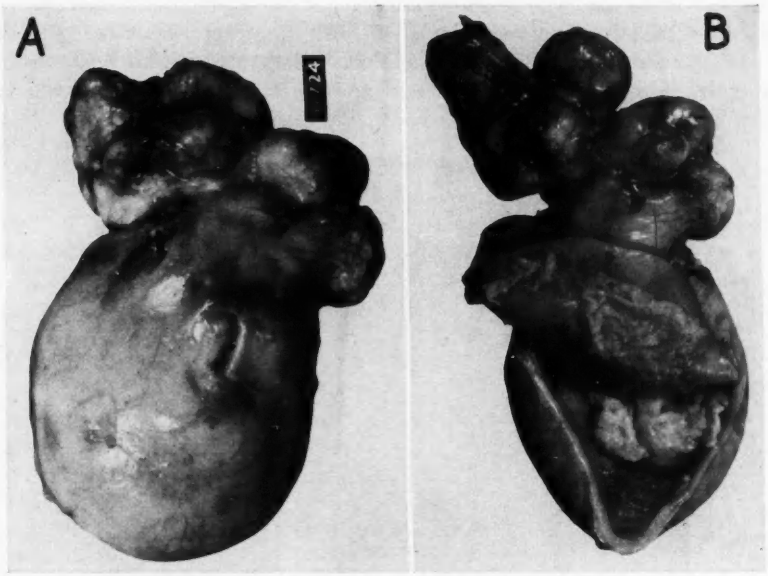

FIG. 3. Case 1. *A*, kidney after removal. No ureter, pelvis, or pedicle present. *B*, aplastic kidney opened, showing interior of large cyst.

Pathological report (Dr. Clyde Culbertson): The specimen consisted of one spherical cyst 9 cm. in diameter, which contained a considerable amount of fibrinous material. Intimately attached to one side of the cyst was a series of individual nodular masses closely associated with one another, and not grossly recognizable as renal tissue. There were no structures present suggesting the normal renal vessels or the ureter (fig. 3).

The wall of the cyst averaged about 4 mm. in thickness. The inner lining was smooth, with some fibrinous material clinging to it in places. Some of the nodular masses were densely fibrinous, others were definitely cystic with a yellowish hemorrhagic mass in the central portion. Microscopic section showed the larger cyst was not lined with epithelium (fig. 4, *A*). On the internal surface there was a sort of granulation tissue with much evidence of old hemorrhage and attached fibrinous material. The cyst wall contained no tubular or glomerular structures, no muscular tissue nor any evidences that it may have been a blood vessel. Some of the more solid masses of tissue showed islands of kidney tissue, tubules and

glomeruli, largely in a state of degeneration (fig. 4. *B*). One or two masses of stratified squamous epithelium were seen in the dense connective tissue, suggesting a teratomatous growth. The yellowish material in the center of certain nodules was xanthomatous in nature and possibly resulted from previous hemorrhage, perhaps during the x-ray treatment. Cultures of the material from the large cyst showed B. coli.

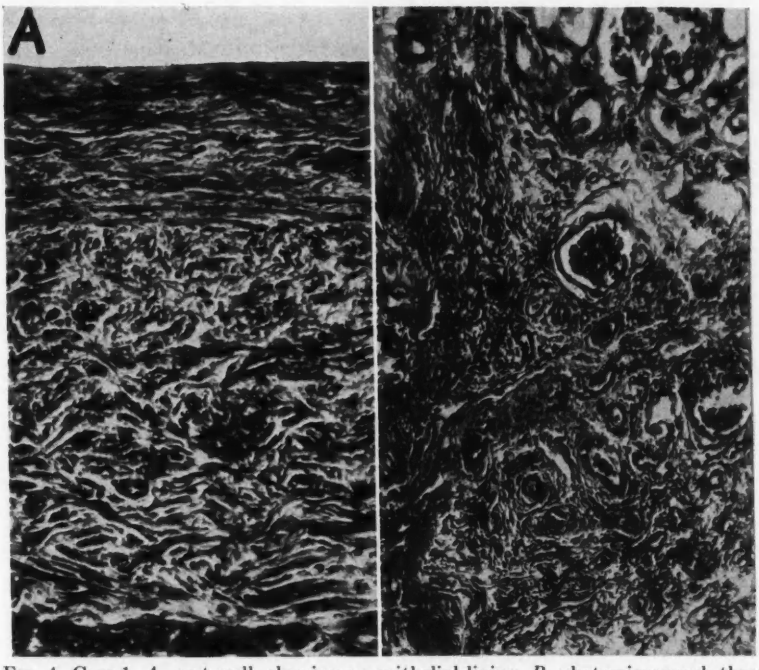

FIG. 4. Case 1. *A*, cyst wall, showing no epithelial lining. *B*, photomicrograph through solid portion of kidney.

Frequent follow-up examinations have been made since the operation. Intravenous urography in 1943 and 1944 again showed good visualization of a right kidney, without evidence of any dye eliminated on the left side. He was last seen on December 31, 1948, at which time his urine was free of pus, his hemoglobin was 11 gm. and his white blood cell count was 9,600. He was having no symptoms.

Case 2. The second case we wish to present is one with a bosselated, multicystic mass in the left renal fossa without a pelvis or ureter. It is of special interest because of its normal location in spite of the absence of a ureter, pelvis or any semblance thereof, notwithstanding the supposed necessity for a ureteral bud as the sine qua non in the embryologic ascent of the kidney from the caudad position to its ultimate site in the upper lumbar region. Its gross appearance was not too unlike that of a cluster of grapes (fig. 5). It lay in the left renal fossa. No struc-

ture was present in any way resembling a normal or diminutive kidney. No pelvis or ureter was present. No definite vascular pedicle was present although several small vessels were clamped at the upper pole when the mass was removed. No left ureteral orifice was present though the trigone was symmetrical. Histologic examination showed glomeruli and rather undifferentiated tubules (fig. 6, *A*)). There was no gross evidence of any recognizable renal parenchyma. In these respects this case would seem to fulfill the prerequisites of renal aplasia as defined by Gutierrez,[3] and Nation.[4] Embryologically, the specimen would represent metanephric tissue with extreme cyst formation, no normal parenchyma, and total disappearance of a one time imperfectly formed ureter and pelvis.

FIG. 5. Case 2. Aplastic kidney removed, hilar side; no vessels, pelvis or ureter

The patient was a white female, aged 5 months, who was first seen in the outpatient department of the Methodist Hospital on April 26, 1948. She was a 7-months premature baby who was in an incubator for 7 weeks. There were no other relevant factors in the patient's past history or family history. She had no complaints and had not been ill. Several weeks before, her pediatrician, Dr. Harold Stadler, had observed a mass developing in the left upper quadrant which seemed to increase in size. A renal tumor was feared. There was no hematuria. There was normal weight increase.

Physical examination revealed a well developed child of 5 months, in no apparent distress. The head, neck and chest were normal. In the left upper quadrant of the abdomen a bosselated, ballotable mass was present about 10 cm. in

[3] Gutierrez, R.: Surgical aspects of renal agenesis. Arch. Surg., **27:** 703, 1933.
[4] Nation, E. F.: Renal aplasia. J. Urol., **51:** 579–586, 1944.

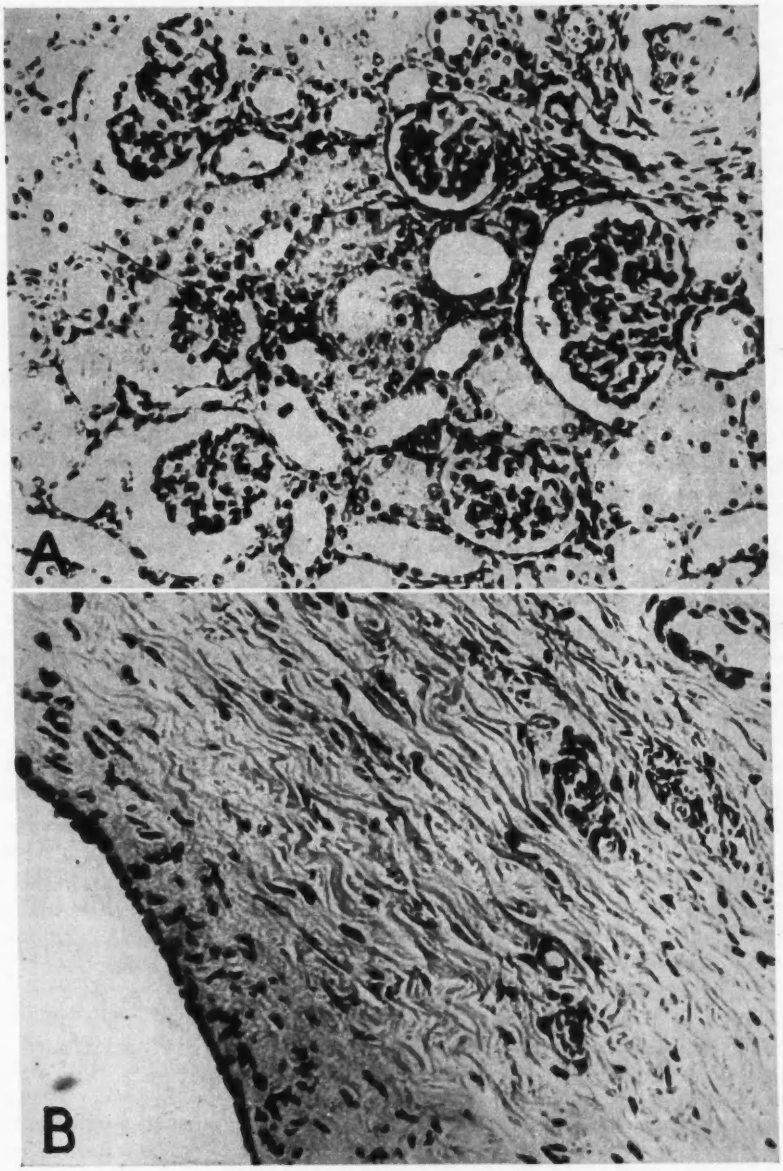

FIG. 6. Case 2. *A*, photomicrograph of more solid portion of aplastic kidney. *B*, photomicrograph through cyst wall, showing epithelial lining.

diameter. It was freely movable and not tender. Its consistency suggested fluid contents but was not flabby. Urinalysis was normal except for a few hyaline and 1 granular cast. Mazzini was negative. The nonprotein nitrogen was 34 mg. per cent. Hemoglobin 7.8 gm. Red blood cells 3,150,000, white blood cells 6,700, with 48 per cent polymorphonuclear leukocytes, 50 per cent small lymphocytes, and 2 myelocytes.

Two cystoscopic examinations showed a contracture and elevation of the vesical orifice (slight), normal right side of trigone and ureteral orifice, and no left orifice. The trigone was symmetrical. The right pyelogram was normal as was the plain x-ray, except that both films showed a soft tissue mass in the left renal fossa.

On May 6, 1949 a provisional diagnosis of cystic left kidney was made and the left loin explored under ether anesthesia. Good general appearance of the child, physical consistency of the mass, and absence of the left ureteral orifice prompted this diagnosis rather than tumor. Upon retraction of the fascia very little perirenal fat was observed. Gerota's capsule was not well developed. Our first view of the kidney, which was easily obtained with little dissection, suggested a polycystic kidney (fig. 5). However, upon dissection of the kidney from its adjacent moorings it became apparent that it was not a true kidney but a collection of closely knit cysts. The pelvis and ureter were not found in spite of careful search. The posterior and anterior portions of the mass were dissected, starting at the lower pole, the tissues wiping away easily with dry gauze. When we had all but a small portion of the mass free at its upper mesial attachment a clamp was applied and the structures cut and ligated as a matter of tradition rather than necessity.

The child had a pre- and postoperative transfusion. She also had a postoperative tracheobronchitis, and the ensuing cough resulted in a partial separation of the incision which healed with hernia. She also had temporary postoperative distention which promptly subsided. Postoperative febrile reaction subsided in 3 days. She was discharged on May 16, 1948, ten days after operation, in excellent condition and has remained so since except for the hernia. Christian Science influences prevent its repair.

Pathologic report by Dr. Horace M. Banks was as follows: "The specimen consists of a multicystic mass 10 by 7 by 5 cm. in size (fig. 5). Careful dissection reveals that these cysts are single masses with thin walls, and do not appear to communicate. They are 0.5 to 4 cm. in size. Deep in the mass there is denser tissue which could represent embryonic renal parenchyma (fig. 6, *A*). Tissue section here shows islands of renal parenchyma separated by fibrous connective tissue. Tubules and glomeruli are scattered indiscriminately throughout. This parenchyma is highly differentiated and appears to be within normal limits except that the tubules are all small and similar with low cuboidal epithelium. Section through the wall of the cyst (fig. 6, *B*) which is quite thin, shows loosely organized fibrous connective tissue in which are found a few structures representative of tubules. The lining membrane in places is absent, in others is a single cell epithelial layer. Fluid from one of the cysts was pale, clear yellow in color and contained 45 mg. per cent of urea, total protein 1.06 per cent and specific gravity of 1.009."

The appearance of the gross specimens and the clinical findings in these 2 patients were quite dissimilar. However, while identical structures were involved in each child, the abnormal development occurred at approximately the same period of foetal life, and the malformations varied only in degree. The embryological fault responsible for the abnormal growth was similar in each instance and was primarily an error in development of the early conducting channels of the excretory system. Any abnormal development of the renal blastoma was purely secondary.

While each excretory organ arising from the nephrogenic cord develops independently, their conducting channels are a common duct. The pronephric duct grows caudad and is continued as the wolffian duct which latter gives rise to the metanephric duct which becomes the ureter.[5] The presence of the lower (caudal) channels depends upon the development of the upper (cranial) ducts. The former will not develop in the absence of the latter.[6] The wolffian duct grows rapidly, extends throughout the length of the nephrogenic cord, and empties into the cloaca at about the 4 mm. stage. This is just before the phronephros has completely disappeared and at about the same time the mesonephros is first detected opposite the upper dorsal segments and long before this latter organ has developed to its caudal limit opposite the third lumbar segment (7 mm. stage). Thus the wolffian body can have but a minimum influence, if any, upon the primary development of the wolffian duct.

The mesonephric duct (the ureteral bud) normally arises from the wolffian duct at the point where it turns abruptly to enter the cloaca (4 to 5 mm. stage). Soon its bulbous extremity comes in contact with the metanephros. This mass of undifferentiated mesodermal tissue is situated opposite the second and third sacral segments. Prior to this union this tissue shows no evidence of specialized action.

As the bulbous end of the ureteral bud invades the metanephric blastoma it divides and subdivides and becomes more intimately associated with this body which immediately responds by an activity which ultimately results in the adult kidney. If at any time subsequent to this union and before the normal kidney is present, further development of the ureteral bud ceases or the rudimentary ureter undergoes atrophy, the remaining metanephric tissue displays a rather constant behavior. It does not progress further toward the adult kidney structure but it tends to atrophy and become cystic. The glomeruli decrease in number, are atrophic, degenerated and displaced. Cystic degeneration of the remaining tubules is frequent. The renal pelvis is eliminated and there is an arrest of development of the renal vessels and the renal pedicle, as found in the normal kidney, is absent.[3]

The cause of the ascent of the kidney is not well understood. While in part it is due to the "diminution of the body curvature during development" it is con-

[5] Felix, W.: In: Keibel and Mall's Human Embryology. Philadelphia, Lippincott, 1912. Arey: Developmental Anatomy. Philadelphia, Saunders, 1934.

[6] Brown, A.: An analysis of the developing metanephros in mouse embryos with abnormal kidneys. J. Anat. **47**: 117, 1931.

Boyden, E. A.: Congenital absence of a kidney. An interpretation based on a 10 mm. human embryo exhibiting unilateral renal agenesia. Anat. Rec., **52**: 325, 1932.

tributed to "in large part by ureteral growth throughout its length." Thus the kidney tends to be pushed cranialward by the growing ureter. Its ultimate position opposite the second lumbar vertebra, attained in the 13 mm. stage, will depend upon a growing ureter until this stage of development is reached. The aplastic kidney may be situated at any point between the pelvis and the loin.

The caudal portion of the wolffian duct, including the ureteral bud, is absorbed into the cloaca and by the 9 mm. stage, each has acquired separate openings. If development continues normally the ureter opens into the bladder at the angle of the trigone, and the wolffian duct into the posterior urethra. A normal trigone indicates a ureteral bud was once present, although the ureteral orifice may not be demonstrated.

Should the point of origin of the ureteral bud from the wolffian duct occur at a higher level than the normal, or should there be abnormal absorption of the uretero-wolffian sinus, the incorporation of the ureteral orifice into the cloaca will be delayed and the union will be at a lower level in the bladder or in the urethra. Under these circumstances there will be an asymmetry of the trigone.

The degree of destruction of the ureter in renal aplasia varies. The entire channel may be obliterated and only a fibrous cord, difficult to detect, will remain (case 2). In other instances destruction of the ureter is incomplete and a portion of the ureter remains patulous but without function (case 1).

The preceding study of the development of the aplastic kidney emphasizes its dependence upon abnormal ureteral growth. It is doubtful if any specialized activity of the metanephric blastoma occurs without the presence of the ureter. Likewise, for the kidney to assume its normal position in the loin, the presence of the ureter during this period of ascent seems necessary.

In case 1, while the ureteral bud may have appeared at the normal time, it was abnormal in its development from the first. There was a precocious cleavage of its bulbous extremity which later resulted in a bifid ureter. Also, the wolffian duct was at fault in that either it gave rise to the ureteral bud at an abnormally high point or it failed to be absorbed into the cloacal wall in a normal manner. Thus the ureter had an ectopic orifice which opened into the posterior urethra. There was an asymmetry of the trigone on the corresponding side. The ureteral bud had contacted the metanephric blastoma and stimulated it to activity, and the ureter subsequently grew sufficiently to contribute its part to the ascent of the primitive kidney to its normal location[7] (6 weeks of embryonic life). However, either because of an inherent weakness in the structure itself, or because of an added factor or factors unknown, retrogressive changes occurred later and there was complete obliteration of the channels of both cephalic branches of the ureter, while the lower half of the ureter had a rudimentary channel (case 1).

In case 2 there was no apparent maldevelopment of the ureteral bud and the kidney had reached its normal position in the loin. However, the aplastic kidney found at operation was merely a group of cysts, no ureter being present, and no ureteral oriffice demonstrable in the bladder on the corresponding side, although the trigone was normal in shape.

[7] Kornblum, K. and Ritter, J. A.: Retroperitoneal cyst with agenesia of the kidney. Radiology, **32**: 416, 1939.

The aplastic kidney is without function. The forces governing development and growth of body structures remain in most part unknown. Likewise, any explanation at this time of their mode of action is incomplete and much a matter of theorizing and speculation. Nevertheless, workers in experimental embryology have made many important discoveries and advances in this field of research. While it is not within the province of this paper to develop this information, for those readers who may be interested a few references to publications concerned with these advances have been added.[8]

The gross appearance and microscopic findings in the aplastic kidney, as in case 1, may closely simulate those found in a wolffian body tumor. The differential diagnosis will be simplified when the independent development of the wolffian body and wolffian duct are recalled. The wolffian body tumor, which is an anomaly of physiological atrophy, need not in its development influence the appearance or growth of the wolffian duct or the ureter. The unattached postperitoneal loin tumor, solid or cystic, of wolffian body origin, will most often be accompanied by a normal functioning kidney and ureter on the corresponding side.

SUMMARY

Two cases are presented which we believe represent failure of normal development of the ureter, with secondary cystic changes of the metanephric tissue. In one the lower end of the ureter was present, in the other, at operation, it was absent. No ureter was found attached to the cystic mass in either patient. In neither case was there any reason to suppose that any of the tissue had ever functioned as a kidney. Both were located in the renal fossa. One was composed of several large cysts with a few small cysts. The other had the appearance of a cluster of grapes. In neither was there any evidence of pelvis, calyx or collecting tubules.

1711 N. Capitol Ave., Indianapolis 7, Ind.

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DISCUSSION

DR. FLETCHER H. COLBY (Boston, Mass.): We are indebted to Dr. Hotchkiss for showing so clearly the classification of these tumors, and particularly the fact that simultaneous bilateral testicular neoplasms usually arise from lymphoid elements and are classified under the general category of lymphoblastoma.

We have had 2 cases such as this at the Massachusetts General Hospital that I am aware of, both of which were associated with the generalized disease, lymphosarcoma. We have also had, I believe, three bilateral testicular neoplasms of embryonic origin. These tumors have not been simultaneous. One tumor appeared first and subsequently the other testis became involved by neoplasm. The last case under this category is a patient who is now under treatment. He is about 55 years of age. He was operated on at the Peter Bent Brigham Hospital in 1937 by Dr. Quinby. The tumor removed at that time from his left testis was reported of embryonic origin. The patient was well until January 1949 when his other testis became enlarged and was obviously involved in a solid tumor. The original slides from the Peter Bent Brigham Hospital were obtained and compared with our own slides. Both tumors were pure seminoma. The important thing to remember from this paper is the fact that when tumors arise simultaneously in both testes, they are quite likely to be of the lymphoblastoma group; when they arise at intervals, they are likely to be of the embryonic type.

DR. JOHN A. TAYLOR (New York, N. Y.): My remarks will be in regard to Dr. Hotchkiss' paper.

Three years ago, at Stockbridge, I reported 2 cases of bilateral but not simultaneous testicular tumors. The first one was a bilateral seminoma, who is now alive and well 22 years after the first orchiectomy and 17 years after the second. He is working as a newspaper correspondent in Washington.

I cannot understand why the second case is alive. It belongs to that group of cases which Dr. Barringer calls the "imponderables." Seventeen years ago, I removed a left testicle, which was the seat of a teratoma. Postoperatively he had abdominal metastases which responded to x-ray. Four years ago, I removed his right testicle, which was the seat of a seminoma. Postoperatively he had a large metastatic tumor in his abdomen, which caused medial displacement of the ureter and duodenum, and caudad displacement of the large bowel. This responded to x-ray, and he is now well 17 years after the first operation.

I cannot refrain from mentioning the third case I reported with these, because it was a case of chorio-epithelioma. At that time, there was no report in the literature of a 5-year cure of this condition. This boy is now well 12 years after operation and brought his son to see me a few months ago because he thought he was getting a testicular tumor. This proved to be a small hydrocele.

DR. W. H. TOULSON (Baltimore, Md.): I would like to discuss Dr. Baker's patient with the pararenal tumor and show you the slides of a case that I will dis-

cuss in a sketchy way. The patient was a white man, 38 years old, complaining of some vague discomfort in the upper right quadrant. Urinary findings were of no moment. The patient was an upstanding, well-developed individual.

(Slide) This shows you the distortion of the ureter, and the next film (slide) shows you the pyelogram, with the evidence of hydronephrosis. A mass began to develop on this side within the week or ten days that he was undergoing this diagnostic procedure. The mass at first was not apparent but on careful palpation in this neighborhood, it became evident as an indefinite mass and rather solid.

(Slide) This shows the opposite side, which looks reasonably normal.

(Slide) This shows the lateral position of the pyelogram and further evidences of a solid tumor. At this point, we had an x-ray of his chest.

(Slide) This is the x-ray of his chest, which appeared negative. At this time, he was operated on. The mass turned out to be a huge tumor mass, identity of which could not be determined at the operating table, but it surrounded the kidney without growing into the kidney, and with some little difficulty, the kidney could be separated from the mass, and the kidney, which was practically a nonfunctioning one, with very little parenchyma, was removed with sections of the tumor which showed, to everybody's amazement, a seminoma with some embryonal characteristics.

Then we re-examined his testicles, particularly the right side, and we looked at the chart and found, on admission, the testicles had been dismissed as normal, as well as the external genitalia, but even then, after we knew this was an embryonal carcinoma, we felt tiny little things that one could normally call cysts of the epididymis. Anyhow, the testicle was explored, and even at exploration, there was no evidence of anything that you would grossly call an embryonal carcinoma. But the testicle was removed and the laboratory showed the same tissue in the testicle as was found in the tumor.

A few months later, he had another chest film made when he began going downhill from this procedure, in spite of deep therapy (slide), and now you see this nodule appearing in the right upper chest. This induced a rapid pneumonia from which the patient died.

(Slide) The last film I show because it has nothing to do with testicular tumors, but it was picked up in one of our Baltimore hospitals in a patient who had evidences of renal tuberculosis, and it shows very typically what we interpret to be a tuberculous chain of post-peritoneal glands, which gives us some evidence of how these post-peritoneal glands are arranged, and opens to question the operation of dissecting out these glands, whether, even though you remove all palpable glands, you will have got all the metastatic nodules.

THE DEVELOPMENT OF CANCER OF THE PROSTATE AFTER SUBTOTAL PROSTATECTOMY

GEORGE GILBERT SMITH AND (by invitation) LORANDE M. WOODRUFF

We became interested in patients with carcinoma of the prostate who had previously had a prostatectomy, of one kind or another, for benign or supposedly benign hypertrophy. These patients were of two types: 1) those who had been operated upon during a previous hospital admission with the diagnosis of benign hyperplasia and, at a later entry, were found to have carcinoma of the prostate; 2) patients operated upon for what was thought to be a benign condition until the pathologist reported otherwise.

One of us (L. M. W.) reviewed the hospital records of all patients with carcinoma of the prostate admitted to the Massachusetts General Hospital between January 1, 1937 and January 1, 1948. There were 648 patients in this group; of these, 39 or 6 per cent had previously had prostatectomies, either at this hospital or elsewhere, with a diagnosis of benign prostatic hyperplasia. Sixty-two cases or 9.5 per cent were found who had had prostatectomies with the definite preoperative diagnosis of benign hyperplasia, in whose surgical specimens the pathologist found cancer.

During this same period there were 64 patients, 10 per cent of those admitted with the diagnosis of prostatic carcinoma, who had total perineal prostatectomies. This represents a fairly high operability as compared with most other clinics and indicates that the urological staff was on the alert to discover patients suitable for this operation. During the same period approximately 2450 operations were performed for benign hypertrophy.

In the group of 39 patients, augmented by 6 from the private practice of one of us (G. G. S.), who developed prostatic carcinoma following the removal of obstructing prostatic tissue in which no carcinoma was found, the intervals between operation and the discovery of carcinoma were as follows:

9 suprapubic prostatectomies, under 5 years, 4; 5–10 years, 2; 10 years or more, 3.

14 perineal prostatectomies, under 5 years, 4; 5–10 years, 4; 10 years or more, 6.

22 transurethral resections, under 5 years, 15; 5–10 years, 6; 10 years or more, 1.

It seems probable that in 50 per cent of these patients, (those in whom malignancy was not diagnosed until at least 5 years had elapsed), the carcinoma either did not exist at the time of operation or was too small to be recognized. A number of pathologists: Albarran and Halle, Moore, Rich, Muir, Kahler, Baron and Angrist, have reported the finding of areas of unsuspected carcinoma in from 14 to 46 per cent of men over 50 years of age. This is a fact to be considered by all who do prostatic surgery.

In discussing the group of 62 patients whose prostatic tissue after removal showed hitherto unsuspected cancer, we wish to point out the difficulty of di-

agnosing carcinoma of the prostate in its very early stage. An article by Kahler of the Mayo Clinic deals with this phase of the problem. Kahler found that in about 50 per cent of prostates which upon microscopic study proved to be malignant, palpation and gross section of the prostates at the autopsy table failed to enable the pathologist to make the diagnosis. Furthermore, upon examining additional sections of 490 prostates which at necropsy had been diagnosed as benign after routine macroscopic and microscopic study, Kahler found 54 carcinomas (11 per cent).

A number of urologists, among them Swan, Bugbee, Mathé, Young, Barnes, Davis, McGavin, Wade, have reported the incidence of unsuspected carcinoma in patients undergoing prostatectomy for benign hyperplasia. The fact seems well established that in at least 8 per cent of enucleated prostates thought to be benign, carcinoma is found at routine pathological examination of the specimens. Thorough examination of the material, for which few pathological laboratories have the time, should, on the basis of Kahler's work, show at least an additional 10 per cent of malignancy.

It is generally recognized that the tissue removed by transurethral resection often fails to reveal the existence of carcinoma in the prostate. In support of this, we found that, among the patients who developed recognized malignancy of the prostate within 5 years after operation for a supposedly benign condition, there were twice as many in the resected group as in the group subjected to enucleation.

Analysis of the material studied by us shows that some 6 per cent of patients who had had prostatectomies developed carcinoma in the residual prostatic tissue. A number of urologists have reported the finding of carcinoma in approximately 10 per cent of prostates removed for a presumably benign condition; with these figures our statistics agree. If the prostatic specimens were to be subjected to complete examination, it is probable that foci of carcinoma would be found in another 10 per cent.

The clinical significance of small areas of carcinoma which have been discovered in the prostate is not known. The incidence of these areas is certainly much greater than is the incidence of clinical prostatic malignancy, but it is reasonable to believe that some of them will develop and will perhaps cause the death of the patient.

For the above reasons, it is our belief that *in selected cases* of apparently benign prostatic hypertrophy, total prostatectomy should be carried out. By this is meant the removal of the entire prostate, severing the urethra at the apex of the gland, stripping the gland by blunt dissection from the internal sphincter and transecting the urethra at the point where it enters the prostatic canal. We do not mean to imply that every man should have this operation for the sole purpose of preventing the development of carcinoma of the prostate, but we do believe that if a man develops prostatic obstruction which requires open operation, total prostatectomy is the best procedure provided the patient's condition, age, and sexual habits offer no contraindications. No other measure will insure him against death from prostatic cancer. As judged from the present series, at least 15 per cent of the cases of carcinoma of the prostate could have been prevented or cured

in this way. We have seen too many patients return with prostatic malignancy a number of years after a subtotal enucleation or a transurethral resection. The situation is analogous to that which made total hysterectomy preferable to supravaginal hysterectomy because of the possible development of carcinoma in the cervical stump.

Complete removal of the gland is only slightly more difficult than the subtotal operation. It consumes a little more time because of the care that is required in anastomosing the bladder neck to the membranous urethra. The vesicles need not be removed. Convalescence is smoother and usually more rapid than after subtotal enucleation. In the 10 patients upon whom this operation was done because of benign hypertrophy, urinary control has been excellent in all. In about 10 per cent of all our total prostatectomies, stricture at the site of anastomosis has required subsequent dilatation, but has responded readily to this treatment. The bladder function has been remarkably good; the urinary infection has cleared rapidly, the stream has been large, there has been no residuum and rarely any nocturia.

One serious result from total prostatectomy is almost certain impotence. For this reason the situation should be discussed with the patient before operation; those still leading an active sexual life should probably have a conservative enucleation if cancer is not suspected.

We do not advocate this operation in men over 75 years of age. At 75 the average life expectancy is only 6 years; if cancer should develop, hormonal treatment may be expected to give from 3 to 7 years of comfort.

The operation should not be done in patients in whom any of the chronic degenerative diseases are at all advanced. Severe vascular or renal disease, or even marked obesity, is a contraindication. Every case must be considered as an individual problem.

CONCLUSIONS

Six per cent of a series of 648 patients with carcinoma of the prostate had previously undergone subtotal prostatectomies for what appeared to be benign hypertrophy.

In 62 patients in our series and also in a number of series reported by other urologists, prostatic carcinoma was found by the pathologist in around 10 per cent of specimens removed for what was thought by the surgeon to be benign hypertrophy.

The intensive study of prostatic specimens by several pathologists has shown that in approximately 10 per cent of the specimens carcinoma was found which had not been detected by routine pathological examination.

Because of the likelihood that carcinoma may develop in those portions of the prostate which are not removed by subtotal prostatectomy and because of the impossibility of detecting by clinical examination the presence of small foci of carcinoma in 15 to 20 per cent of glands which are operated upon because of benign hypertrophy, total prostatectomy in selected cases of benign hypertrophy is advocated.

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THE INDUCTION OF TRANSPLANTABLE BLADDER CARCINOMA IN INBRED STRAINS OF MICE

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A principal difficulty in the study of carcinoma of the bladder has been that of consistently producing such lesions in a suitable experimental animal. This problem's solution began in 1937 when Hueper and Wolfe first reported successfully inducing papillary tumors of the dog's bladder, both benign and malignant, when large doses of beta-naphthylamine were fed by mouth.[1] In 1943, Bonser[2] published the results of feeding a specially purified beta-naphthylamine to 4 dogs over a period of from 3 to 5 years, and in this period observed histologic changes ranging from simple epithelial hyperplasia of the bladder to anaplastic carcinoma. But by standards of time and expense, the dog is not a suitable experimental animal for the study of bladder cancer.

Working with albino rats, Wilson, De Eds and Cox (1941)[3] found that of 39 rats fed 2-Acetylaminofluorene for 95 days or more, 10 developed carcinoma of the bladder. Feeding the same carcinogen to the CBA strain of mice, Armstrong and Bonser (1944)[4] were successful in inducing malignant changes in the bladder epithelium of 4 mice out of 6 surviving 53 to 65 weeks of treatment. Foulds (1947)[5] found only 25 weeks of feeding 2-Acetylaminofluorene to the R_3 strain of mice was necessary in developing epithelial tumors of the bladder, though the tumors required an additional period of from 14 to 59 weeks to become demonstrable. About one-half of his treated male mice developed such tumors but none occurred in the females.

2-Acetylaminofluorene however, is not a specific bladder carcinogen, for malignant tumors also developed in other organs. Furthermore, the induction of carcinoma of the bladder in the normally situated bladder of small experimental animals has the distinct limitations of time and space. The limitation of time is that the individual tumor has only the life span of the experimental animal in which to grow. The limitation of space is that imposed by the bladder in situ—the occurrence of carcinoma can scarcely be determined until autopsy after death or sacrifice of the animal.

These limitations do not apply to a method we wish to describe in this report—a method in which carcinoma of the bladder has been induced in inbred strains of mice as a subcutaneous implant which continues its growth as a homologous subcutaneous transplant.

[1] Hueper, W. C. and Wolfe, H. D.: Am. J. Path., **13**: 656, 1937.
[2] Bonser, G. M.: J. Path. & Bact., **55**: 1, 1943.
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[4] Armstrong, E. C. and Bonser, G. M.: J. Path. & Bact., **56**: 507, 1944.
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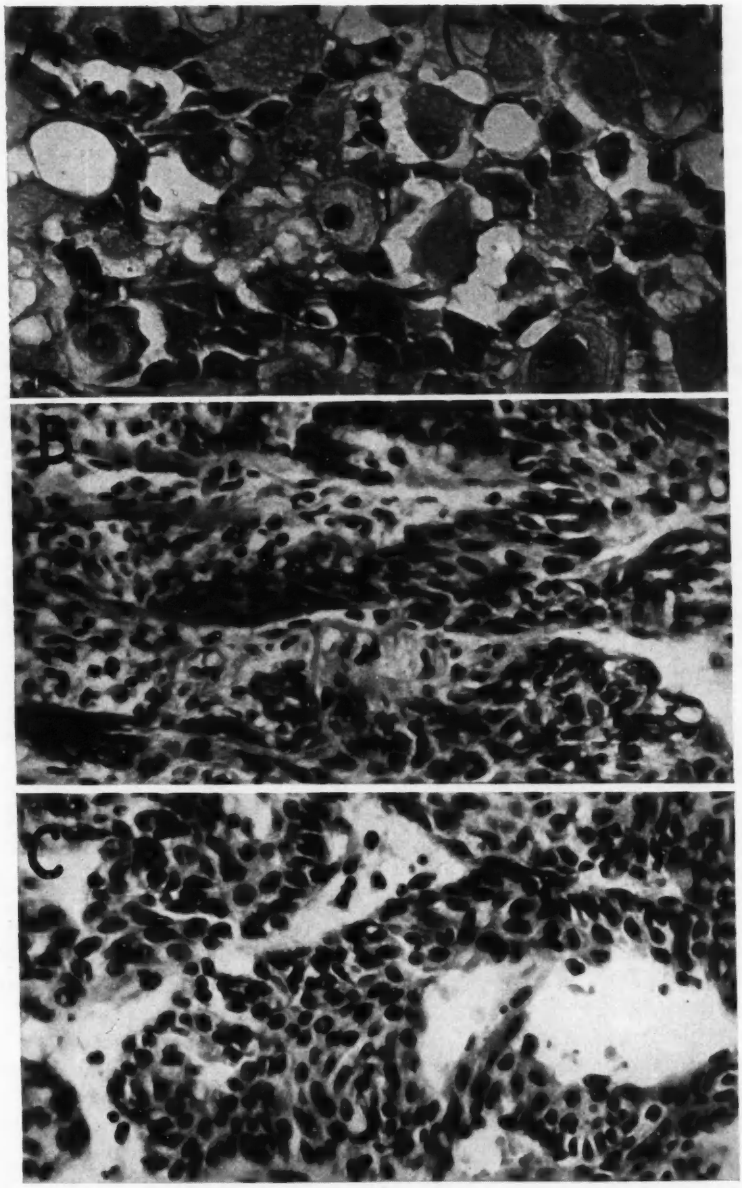

FIG. 1. *A*, tumor No. 32, C_3H mouse, third transplant generation (× 650); an undifferentiated carcinoma. *B*, tumor No. 148, C_{57} mouse, 4½ months after induction (× 400); papillary tongues of epithelial malignancy project into subcutaneous tissue of host. *C*, tumor No. 148, C_{57} mouse, 4½ months after induction (× 400); malignant cells have tendency toward papillary arrangement.

The first successful attempt to induce a series of transplantable tumors arising from adult tissue and capable of growing as homologous subcutaneous grafts was reported by Horning in 1946.[6] Horning induced and maintained by transplantation glandular carcinoma of the prostate gland in inbred Strong A mice. Our application of the Horning technique to the problem of inducing transplantable bladder carcinomas is described below.

The bladder is removed from a young mouse of an inbred strain and the entire mucosa, with portions of adherent submucosa, immediately dissected from the bladder wall under a dissecting microscope. This isolated mucosal layer, with its adherent submucosa, is wrapped around crystals of 20-methylcholanthrene, care being taken that only the epithelial portion of the mucosa comes into contact

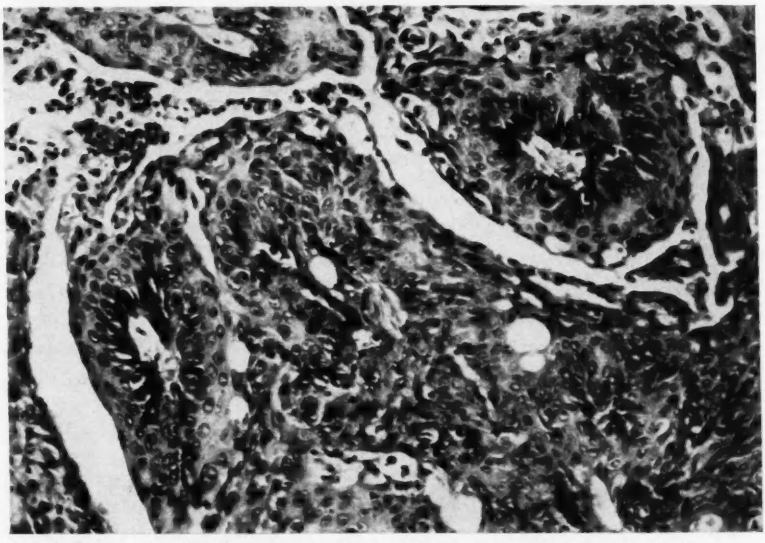

FIG. 2. Tumor No. 148, C_{57} mouse, in its second transplant generation (× 400); squamous cells are well differentiated, showing keratin formation.

with the carcinogen; by means of a special trocar the mucosal wrapping thus produced is then implanted under the abdominal skin of a host animal from the same inbred strain—in our experiments, a litter mate. Sterile technique is maintained throughout.

After the tumor has grown to transplantable size, it is excised, minced, and implanted subcutaneously into the desired number of mice from the same strain.

When carcinogens induce tumors by direct tissue contact the tumor type developed depends upon the nature of the tissue cell contacted. In our earlier work technical errors permitted the carcinogen to contact cells other than those of the bladder epithelium. This error resulted in sarcoma arising from the non-epithelial cells contacted, since in the mouse sarcomas are easier of induction and more rapid in their growth than carcinomas. These technical errors are not yet com-

[6] Horning, E. S.: Lancet, **2**: 829, 1946.

pletely eliminated although the method is yielding a higher percentage of carcinomas as we become more proficient.

RESULTS

In this work we have used three inbred stains of mice. The Strong A strain yielded two carcinomas, both currently in their third transplant generation, from twenty-three attempted inductions. Our efforts in strain C_{57} were productive of only one transplantable carcinoma in 32 trials. In C_3H mice we achieved eleven transplantable carcinomas out of 65 attempts.

After the first transplantation there has been no change in the histologic pattern of these epithelial malignancies through as many as eleven transplant generations. In all strains, the development of the carcinoma in its host to transplantable size has required from two to four and one-half months. Sex, either of donor or host, has not appeared to influence development of the carcinomas.

SUMMARY

The Horning technique has induced and perpetuated in mice a constant type of epithelial bladder cancer beyond the life span of the individual experimental animal. It has brought carcinoma of the bladder to a readily accessible area beneath the skin where the influence of experimental variables may be easily measured. With refinements in technique making predictable an expected per cent of carcinomas, inquiry into inhibition of vesical carcinoma becomes feasible. The technique described offers an improved animal test object for investigation of carcinoma of the urinary bladder.

Acknowledgments: We wish to thank Dr. Margaret Reed Lewis for her aid and advice.

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THE BIOLOGICAL BEHAVIOR OF TRANSITIONAL CELL PAPILLOMA OF THE BLADDER

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It is necessary to study the life history of any tumor in order to become acquainted with its behavior. So far no one has given the life history of the transitional cell papilloma of the bladder. Interest in the minute characteristics of this tumor is accelerated by the controversial views with respect to its benignancy and malignancy long held by histopathologists and clinicians, although neither have definitely proved their hypotheses. We have taught and are responsible for teaching that a majority of bladder papillomas, if not all of them, are potentially malignant tumors; and that we may expect that the histologically benign papilloma of the bladder, if untreated, will transform itself into a readily recognized cancer whose malignant changes are characterized by irregularities of the size, shape and arrangement of cells, nuclei rich in chromatin, mitoses, giant cells, multinucleated cells, and fusion of the adjacent papillae with infiltration of the stalk and of the bladder wall. Our knowledge concerning the behavior of this tumor is limited to the fact that 30 to 40 per cent of them never recur after initial fulguration and the assumption that 60 to 70 per cent either return in great numbers, sometimes simulating the parent tumor, or become invasive and are histologically malignant.

It is logical to believe that those transitional cell papillomas of the bladder which are treated once and never recur belong to a benign tumor group, because of their cellular structure and the complete control of their growth by a relatively simple form of treatment. Does the bladder papilloma which is free from the stigma of histological malignancy really change its cell pattern; and, if so, how frequently? Jewett and Blackman, in their study of infiltrating tumors of the bladder, found a uniformity in the cell pattern in 80 per cent of the papillary and epidermoid cancers. If the cell patterns of bladder tumors do not change then why do we see transitional cell papillomas of the bladder, some of which are benign and others malignant with respect to their biological behavior and their pathology? Do we have two types of transitional cell papillomas of the bladder, one beginning as a benign tumor and remaining a benign tumor, and the other, although appearing benign in its early stages, actually beginning as a malignant tumor and, as it develops, manifesting its malignant characteristics clinically?

It is the purpose of this paper to present the results of our study of the life history of the transitional cell papilloma of the bladder as a fractional part of a critical survey of all bladder tumors treated in our clinic during a 27-year period. Of the total of 407 patients with bladder tumors only 3 patients, or less than 1 per cent, were lost in the follow-up from the onset to the present time or to the death of the patient. All cases in which accurate descriptions of the bladder tumor were

not recorded or sufficient and adequate biopsy material had not been obtained were deleted. Among the total of 407 bladder tumors 109 were classified as transitional cell papilloma or benign papilloma or papillary cancer, grade I, according to the standards of classification by Ash and Broders. Our interpretation of a transitional cell papilloma of the bladder is a papillomatous tumor with villi covered with transitional epithelial cells similar to the cells of the bladder with a central stalk of fibrous tissue and blood vessels. The epithelial cells are all uniform and regularly arranged on a definite basement membrane which is not infiltrated. Papillomas showing any change in the regularity in the size, shape and the arrangement of the cells, any changes in their nuclei or fusion of the villi were considered papillary carcinoma and were not included in this paper.

INCIDENCE

Of the 109 cases of transitional cell papilloma, 80, or 73 per cent, occurred in males and 29, or 27 per cent, occurred in the female, a ratio of 3 to 1 in favor of the male. The youngest male patient was 23 years, while the youngest female was 42 years. About 10 per cent of the tumors in the male occurred under 45 years, while only 1 female was under 45 years. Eighty-six per cent of the tumors were found in male and female patients between the ages of 50–80 years; while the average age of the male patient was between 60–70, and of the female, between 55–65 years. The predilection of these tumors to develop and grow in the male bladder would seem more than a coincidence and raises the question of hormonal influence.

Transitional cell papilloma was found to be single in 56 per cent and multiple in 44 per cent of the cases. While the Bladder Tumor Registry reports that only one-third of papillomas are found on the trigone, in almost one-half of this series the tumors were located on the trigone; next in location was the posterior wall, and the anterior wall was the least commonly involved. The actual size of the tumor was stated in 81 cases: 7 per cent were more than 5 cm. in width, 73 per cent between 2 and 5 cm., while 20 per cent were less than 2 cm.

In order to be of value in this life history survey of the transitional cell papilloma it was calculated that papillomas should be studied for more than a 3-year period; consequently all cases of patients who were followed less than 3 years, who died within the 3-year period from the first diagnosis, or who had infrequent follow-ups were excluded. This left a group of 52 cases, 75 per cent of which were followed over 5 years, 32 per cent over 10 years, and 4 over 20 years, with the longest observation being 26 years.

The study of these cases revealed that transitional cell papillomas of the bladder followed one of four patterns of growth:

1) 30.8 per cent began as a single or a multiple tumor, or a few sporadic tumors, occurring over a short interval of time, with no subsequent new growth after treatment.

2) 50 per cent exhibited a slow rate of growth, less than 10 new growths per year, and the tumor began as a single or multiple tumor with growth-free intervals of 2 to 8 years.

3) 11.5 per cent showed a high rate of new growth averaging more than 10

tumors per year over many years. One patient in this group, first seen 6 years ago, has already had 393 new growths, a rate of 65 per year, and the tumors are continuing to recur at atomic speeds reaching as high as 93 new growths in one year.

4) The least common growth pattern was a mixed type showing both high and low rates of new growth and comprising only 5 per cent of the cases.

It is not always easy to make a differential diagnosis between the histologically benign group and the early histologically malignant group. Great care was taken not to include slow-growing carcinomas; and cases that did not have one or more biopsies showing a benign tumor over a period of time prior to the malignant change were excluded. Certainly the cystoscopic picture can not be depended upon, nor can the biopsy of one area only, for a biopsy of the superficial part of the tumor may show undeniable evidence of a benign transitional cell tumor, while a biopsy of the base may show a tumor of carcinomatous character. Melicow specifically pointed out this observation in some of the papillomas which were removed surgically; so that an adequate specimen, including the base of the tumor, should of necessity be examined. Tumors showing histologically malignant changes in any portion were classified as carcinomas. One must be on his guard, for clinically one finds tumors which do not respond well to fulguration or which tend to recur and provide evidence of a malignant tumor rather than a tumor of benign quality. An example of misinterpretation of biopsies of recurrent tumors is found in the history of a woman who originally had a few small sessile growths which had a tendency every 3 to 6 months to form 6 to 10 new growths which after a period of 4 years metastasized as a squamous cell cancer to the cervix, uterus and adnexa within 5 months; yet the tumors within the bladder cavity all these years had appeared cystoscopically to be completely destroyed by fulguration at each visit of the patient. In reviewing numerous biopsies taken throughout the 4 years all showed giant nucleus formation scattered irregularly among the regularly arranged transitional cells.

There were 8, or 7.3 per cent of cases, among the 109 transitional cell papillomas which became malignant, 1 in 3 years and 11 months, 3 in 5 to 10 years, and 4 in 10 to 15 years (table 1). Five became papillary carcinomas, 2 squamous cell carcinomas and 1 anaplastic carcinoma. To follow Jewett's classification of groups according to infiltration, 3 of the papillary carcinomas belong to group A and 2 to group C. The three group A patients were followed at frequent intervals, while the two in group C failed to return until 3½ years. Our observations would indicate that a few of these tumors have a tendency to take on carcinomatous characters probably very gradually. Tumors which appear to change suddenly to malignancy very likely did not have adequate biopsy or a critical study of the cellular structure in the early biopsy specimen.

Does this study of the life history of the transitional cell papilloma of the bladder give any clue as to its future behavior? The answer is in the affirmative if the operator will biopsy each new growth or group of new growths. Any change from the benign to the malignant phase will be first manifested by changes in the size, shape and staining qualities of the nucleus and nucleolus, presence of numerous small cells or giant nucleated cells and loss of regularity of cell arrange-

ment. It appears in this study that as long as there is no cell change found in frequent and adequate biopsies the tumors behave like benign tumors. The longest case of follow-up is for a 26-year period, during which time the various biopsies of the tumors have not showed any histological change. In this case tumors have recurred one or two in number every 1 to 4 years. On the other hand, of those patients who showed a fast rate of growth of new tumors, that is, more than 10 tumors per year, 66.7 per cent developed carcinomas. Of those patients who grew new tumors slowly only 6.6 per cent developed carcinomas. In the group of patients with slow-growing tumors who developed carcinomas all had long intervals without new tumor growth prior to their becoming malignant. Any transitional cell papilloma of the bladder which shows giant cells, even though the cell arrangement is regular, should be considered potentially malignant and demands adequate biopsies at each visit.

TABLE 1. *Cases of bladder papillomas that became carcinomas*
8 cases, or 7.3%

Type and group of carcinomas that developed

TYPE	GROUP			
	A	B	C	Metastatic
Transitional cell carcinoma	3		2	
Squamous cell carcinoma			1	1
Anaplastic carcinoma			1	

Length of time required for change to carcinoma in the 8 cases

TIME IN YEARS	NUMBER OF CASES
3–5	1
5–10	3
10–15	4

Bladder papillomas may be found in association with other malignancies. Nine patients in these 109 cases, or 8.3 per cent, had other malignancies. Four had carcinomas of the breast, one of the uterus, one of the rectum and two of the kidney, while one had two malignancies, namely cancer of the cervix and multiple myelomas.

The heterologous transplantation of the bladder papilloma into the eye of the guinea pig with 4 takes made us suspicious early in our research that all bladder papillomas were carcinomas. These transplants seem to develop only for one generation and could not be made to grow heterologously in the second generation. One hundred and twenty-seven transplants have been made without further takes. One must now conclude, after such extensive experience of unsuccessful heterologous growths, that the original hypothesis is not justifiable and that these tumors in general do not have the character of autonomous independent growth.

The transitional cell papilloma of the bladder produced symptoms almost

identical with cancer of the bladder (table 2). Gross hematuria is the most common symptom, as will be seen in the accompanying table. Frequency, nocturia, dysuria, urgency, hesitancy, diminution in the stream, acute retention, weight loss, pain in the abdomen and loins, and in some cases incontinence of urine are among the other recorded symptoms. There is no one symptom which is pathognomonic for papillomas of the bladder.

The behavior of these tumors in response to treatment is illustrated by the summation of the various therapeutic measures applied. As would naturally be expected over this 27-year period numerous methods of treatment were used for these 109 cases. Cystoscopic fulgurations, as recommended by Beer superseded all other treatments, being used 620 times. Cystoscopic implantation of radon or surface application of radium was applied 35 times. Suprapubic cystostomy with cautery excision of the tumor was employed 27 times and in 9 cases radon was implanted at the same time. The response of papillomatous tumors to treatment

TABLE 2. *All symptoms of bladder papillomas and carcinomas*

ALL SYMPTOMS	PAPILLOMAS, 109 CASES		CARCINOMAS, 209 CASES	
	Number	%	Number	%
Hematuria (gross)	92	84.4	183	87.5
Frequency and/or nocturia	60	55.0	154	73.6
Pain on urination	20	18.3	47	22.5
Weight loss	12	11.0	33	15.8
Urgency	10	9.2	20	9.6
Hesitancy	7	6.3	16	8.0
Diminution in stream	6	5.5	11	5.2
Acute retention	6	5.5	10	4.8
Abdominal pain	5	4.6	6	
Pain in loin	5	4.6	5	
Incontinence	2	1.8	8	
Miscellaneous symptoms	5	4.6	10	4.8

by fulguration is many times significant, for on applying the fulgurating electric current they are readily destroyed while the malignant tumors are resistant and more difficult to coagulate. Segmental resection of the bladder, deep x-ray therapy and total cystectomy were less commonly used. The results would indicate that fulguration is by far the most effectual treatment but that there is much room for improvement of the treatment, depending upon which pattern of growth the tumor develops. One can expect by cystoscopic fulguration 83 per cent 3-year control, 66.7 per cent 5-year control, 42.5 per cent 10-year control and 30.5 per cent permanent control. The responsibility of controlling rapid recurrences of new growths of the bladder is great, and the subjection of the patient many times a year to fulguration treatments seems unjustifiable and furthermore the chances for the tumor developing into a cancer are 66.6 per cent. When repeated biopsies show cellular changes indicating malignant characters more radical treatment than fulguration is indicated. For those cases which develop more than ten tumors per year a total cystectomy is advocated. The be-

havior of these tumors to hormones was not observed. Grant and Lich theorized that these tumors embryologically and histologically were similar to those of the prostate but did not with hormonal treatment of a few cases obtain satisfactory results. Haines and Miceli noted only mild response in the male patient with the use of stilbestrol.

SUMMARY

This study of the life cycle and behavior of the transitional cell papilloma of the bladder would indicate that the majority of them behave like benign tumors. They behave and remain similar to benign tumors as long as their cells are free from any malignant changes. By heterologous transplantation they do not show the inherent character of autonomous and independent growth. Many of the so-called benign papillomatous tumors of the bladder, in review of their histopathology, contain minute evidence of malignant character and should not be called benign tumors but malignant tumors. There is one chance in fourteen of their becoming malignant. They prefer to develop and grow in male bladders with the ratio of three to one and may be influenced by hormonal factors. They may take one of four patterns of growth, and the therapeutic control of their growth should be applied accordingly. Frequent biopsies are imperative for the determination of any changes in their cellular structure. Fulguration is the therapeutic agent of choice, but if new growths recur to a greater number than 10 per year a total cystectomy is recommended until some other more effectual means of control is found. The behavior of the transitional cell papilloma of the bladder can be predicted with a fair degree of accuracy by adequate and frequent histological study and consideration of the rate of growth.

The author wishes to express his appreciation of the services of Mrs. M. Jack in the follow-up of patients and the assistance of Dr. Philip Viscidi for his compilation of case reports and review of the pathological slides.

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DISCUSSION

DR. EDWIN DAVIS (Omaha, Neb.): I do not think we should pass these three papers without comment. They were all well presented, concise, informative, and listened to with profit.

Unless I misunderstood Dr. Smith, a critical postoperative pathological study will reveal unsuspected carcinomatous foci in 15 to 20 per cent. Thanks to Dr. Smith, I think I shall do more total prostatectomies, being guided, however, by his listed contraindications.

Dr. Hughes has presented an exceedingly interesting study which must have required a great deal of technical skill and patience, and it is studies such as these which we hope may eventually lead to a better knowledge and understanding of the etiology of at least some cases of clinical or spontaneous bladder tumors, in addition to the anilin tumors; in other words, there may be more bladder tumors susceptible to explanation upon a chemical carcinogenetic basis.

We are also indebted to Dr. Deming. It is the strange behavior habits of bladder tumors which lead us to a consideration here of a possible chemical carcinogenetic origin—and by strange habits, I refer to the tendency toward multiplicity and recurrence. Probably "recurrence" is the wrong word, because a tumor may be destroyed in the southeast corner of the bladder and then appear in the northwest corner.

We must therefore think of a possible papilloma-forming tendency which this patient has. I use that expression for lack of a better one. Perhaps we may explain these tumors on the basis of a chemical carcinogen which masquerades as an innocent substance, or possibly a carcinogen of endogenous or physiological origin.

DR. GEORGE R. LIVERMORE (Memphis, Tenn.): Dr. Deming's report of 30 per cent malignancy in papillomas of the bladder bears out the contention that these tumors are potentially malignant. Such cases should not be treated by fulguration. In the early stages we have our best chance to cure. Therefore, I give a course of deep x-ray for 30 days then remove the growth by segmental resection and then implant radium needles in the bladder.

All our armamentarium should be used in the early stage rather than fulgurate and wait for recurrences before resorting to drastic measures.

In regard to Dr. Smith's paper, I have had cases in which carcinoma has developed in the prostate following prostatectomy. I remember 1 case that occurred 6 years after prostatectomy and another 14 years.

DR. ROGER C. GRAVES (Boston, Mass.): Dr. Smith's excellent and thought-provoking paper brings to my own mind a situation that has confronted me and that perhaps has confronted you, in which a pathological report of carcinoma of the prostate is received after the enucleation of a supposedly benign gland. I do not refer to the finding of a small focus of cancer surrounded by benign hyperplasia, but to the report of frank cancer which has been unsuspected.

I have an idea that this may occur in the case of a very anaplastic tumor that has not presented the usual characteristics of carcinoma, on rectal examination.

I recall four such problems that I have had in recent years, the first one during the war, when I enucleated the prostate on the supposition that it was benign, in a second-stage suprapubic prostatectomy. The report was carcinoma. I felt very remiss, and wondered what might be done. A few days after operation, we passed a Foley catheter and drew the inflated bag down into the prostatic cavity, and then approached that through the perineum as an artificial, temporary prostate. The prostatic capsule and the seminal vesicles and the neck of the bladder were removed as in total perineal prostatectomy and much to my relief the patient has almost perfect control of urine. One other case, more recent, was somewhat similar and turned out equally well. In two other cases in which carcinoma had been suspected clinically, the pathologist failed to confirm the diagnosis on the perineal biopsy. In one of these cases no prostatectomy was done at that time; in the other a subtotal perineal prostatectomy was performed. When later, final reports of cancer were received, the same procedure was carried out in each instance and a total perineal prostatectomy was done, removing the capsule and the seminal vesicles and the neck of the bladder. The results were good and a very satisfactory degree of urinary control was obtained.

Dr. David M. Davis (Philadelphia, Pa.): I would merely like to add to these reports a few other instances, two that I can recall in which prostates suspected of carcinoma were operated upon, pieces removed for biopsy, and a negative report returned. Consequently, conservative perineal prostatectomy was carried out. Further study of the removed sections showed that the original pathological report was incorrect. In both of these cases, within a week, the incision was reopened and radical perineal prostatectomy carried out successfully.

In the 2 other cases radical perineal prostatectomy was carried out within a week to 10 days after sections removed at transurethral section showed unsuspected carcinoma. In 2 other cases radical perineal prostatectomy was carried out upon patients in whom early and small carcinomatous nodules were found on routine examination long after transurethral resection, one of them 4 years after the resection, the other 5 years after the resection; so we have to think, as Dr. Smith says, about these complicating situations.

Dr. George G. Smith (Closing discussion): In regard to the question raised by Dr. Emerson Smith as to where I think the original site of the carcinoma in the prostate is, I must plead complete ignorance. I was brought up in the days when Geraghty stated that three-quarters of all cases began in the posterior lobe, and I went very comfortably on that assumption for a good many years, and it did seem, on cross-sectioning the totally removed prostates, that the major part of the growth was in the posterior lobe. But now, I think, with greater interest in carcinoma of the prostate and more complete investigation by different pathologists who have been interested in it, such as Kahler, it has seemed pretty well demonstrated that the tumor may be multiple in point of origin. It may occur—I think Kahler found in 13 or 14 per cent, as I remember—in the hyperplastic portion, and there certainly have been cases where carcinoma was found in the

enucleated section of the gland, that have never developed any tumor of the prostate after that, within a reasonable period of observation. I saw one such case not very long ago. Therefore, I hardly know what to say about that.

I do think that the only cases we can feel on rectal examination are those in which the tumor has developed from the periphery of the gland. We cannot find the central tumors. And that leads me on to what Dr. David Davis has said about the biopsy in these cases. I have about come to the conclusion that if, upon exposure of the prostate perineally, with the preconceived idea that the gland was malignant, thorough palpation of the gland at that time bears out the previous finding, and if the pathologist comes back and says, "No tumor is found" in a reasonably good biopsy specimen, I say that you can go ahead and take out the prostate, because I have had a number of cases where the gland has proved to be malignant on later removal. Dr. Davis has reported these, and I know that Dr. Leadbetter and all of us have found cases of that type.

I feel that this doing a total perineal prostatectomy in apparently benign cases is something that should be seriously considered, and I am going to do it more and more in selected cases. It is just too bad when these patients, on whom you have done an enucleation, come back four, five or ten years later with carcinoma of the residual prostatic tissue.

I feel very much honored to have been on the program with two such excellent papers as Dr. Hughes' and Dr. Deming's. I enjoyed them both, and I think they are both gems.

Dr. Clyde L. Deming (Closing discussion): I would like to compliment Dr. Hughes on his approach to the tumor problem of the bladder. It is one more way to produce and grow a tumor of the bladder. Your aim, and mine, in our work together, is to find the etiology of the tumors of the bladder, and I believe that through these efforts, sometime in the near future, we will find out what the cause of bladder tumor is.

TREATMENT OF MALE INFERTILITY: AN EVALUATION OF MEDICINAL THERAPY

ORMOND S. CULP AND DAVID E. BEYNON

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Public demand and time limitations on a busy urologic service have prompted a critical survey of our male sterility cases in the hope of answering two pertinent questions: 1) What studies have the greatest diagnostic value; and 2) has any type of medicinal therapy been effective?

The first 200 patients with complete follow-ups have been reviewed. The wives were examined by competent gynecologists. Complete physical examinations were done on all men. Semen studies were made by an assistant resident who assumed this responsibility for 12 months after thorough indoctrination by his predecessor. Several samples were run from each specimen of ejaculate and more than one determination was made on each sample to minimize the flagrant laboratory errors that can occur even after much experience. Standard techniques were used throughout all studies.

Ages of the patients varied from 20 to 49 years. Ninety-four per cent were less than 40 years of age.

Initial sperm counts resulted in 3 types of patients, as shown in table 1: 1) more than 60,000,000 per cubic centimeter, 2) less than 60,000,000 per cubic centimeter, and 3) no demonstrable spermatozoa on repeated examinations. Thirteen wives were thought to be possible factors in the barren marriages. These cases have been omitted regardless of any male abnormalities. All patients with azoospermia also were eliminated. Such cases can be evaluated properly only by testicular biopsy and are not within the scope of this paper. There were 163 individuals who were suitable for sperm studies.

These barren marriages were of 1 to 20 years' duration (fig. 1). Forty-seven per cent of the couples had been unsuccessful for 4 to 6 years.

Sperm data with the greatest promise of value seemed to be: a) motility, b) morphology, and c) average counts.

Only 11 of the 163 patients had persistent lack of sperm motility. More than half of the entire group had at least 70 per cent motile forms. Except for a few isolated cases, motility proved to be disappointing when one tried to explain infertility.

Recognition of abnormal forms depends on so many personal and technical factors that we question the accuracy and value of most determinations, except when made by specially trained observers. Our studies with the electron microscope have made us even more skeptical about accepted morphologic criteria. Only 13 of our 163 patients (8 per cent) had more than the acceptable 20 per cent abnormal forms on routine light microscopy.

Sperm counts can be remarkably consistent if one does enough of them to perfect the technique and minimize errors due to the viscosity of the fluid. Figure

TABLE 1. *Types of cases*

SPERM COUNTS	NO. OF PATIENTS	WIFE DOUBTFUL OR ABNORMAL	SUITABLE CASES
60 millions per cc or more	76	6	70
Oligospermia	100	7	93
Azoospermia	24		
Total	200	13	163

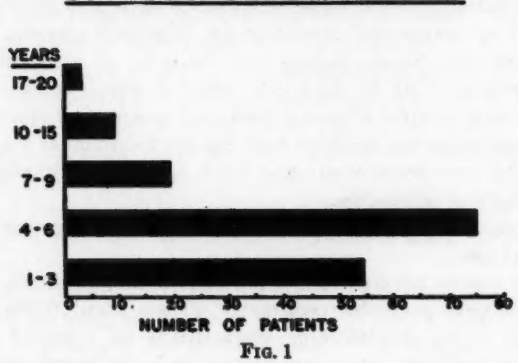

FIG. 1

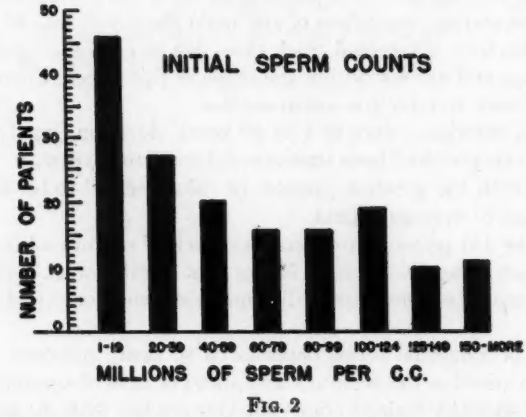

FIG. 2

2 shows the initial averages in this series of 163 patients. The largest group had from 1,000,000 to 19,000,000 per cc, obvious oligospermia.

Thirty-four of the total 200 patients had physical defects capable of influencing the degree of fertility (fig. 3). Three patients had subnormal basal metabolic rates but none of their reduced sperm counts was increased when the basal

metabolism rate reached normal on thyroid extract. Most of the patients with cryptorchidism or testicular atrophy had azoospermia and have been omitted from our analyses.

It is especially noteworthy that no one with a solitary normal testis had a normal sperm count; and that azoospermia prevailed even though bilateral

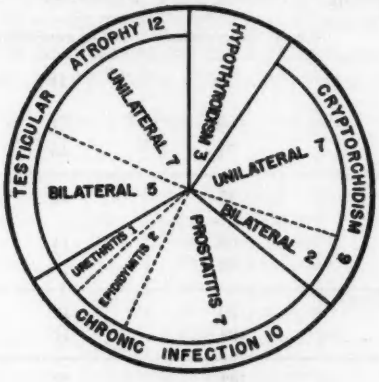

FIG. 3

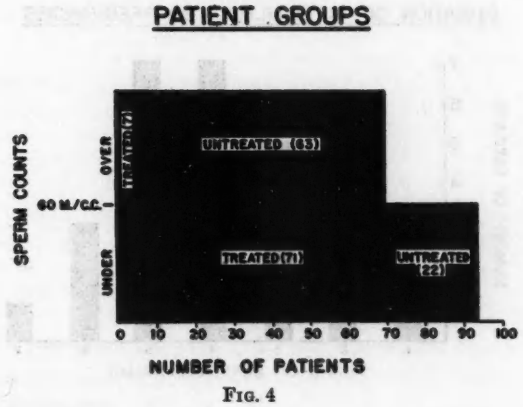

FIG. 4

orchidopexies were performed before puberty. These observations are being investigated further.

Varying degrees of oligospermia accompanied the chronic infections. Only the patient with urethritis developed a normal count after treatment of the infection. Everyone in this category also had some type of drug therapy for his infertility.

Only medicinal treatment will be evaluated in this study. All surgical or instrumental procedures have been relegated to subsequent analyses. As shown in figure 4, 78 patients were treated while 85 received no drugs. Most of the 70 pa-

tients with high sperm counts were merely observed. Seventy-one of the 93 with oligospermia were given some type of medication while 22 were used as controls.

The effectiveness of any therapy can be measured only by the incidence of pregnancy and the alterations in the sperm pictures. Faith in the moral integrity of 163 wives may be naive, especially when one hears of the remarkable ingenuity employed by some devoted wives to avoid crushing the profound ego of their virile but sterile husbands. Furthermore, it is technically impossible to analyze a

TABLE 2. *Distribution of pregnancies*

TYPES OF CASES	TOTAL NO. OF PATIENTS	NO. OF PREGNANCIES	PER CENT
Total treated	78	14	17.9
Over 60 m./cc	7	1	(14.3)
Oligospermia	71	13	18.3
Total untreated	85	15	17.6
Over 60 m./cc	63	11	17.5
Oligospermia	22	4	18.2
Total over 60 m./cc	70	12	17.1
Total oligospermia	93	17	18.3
Entire series	163	29	17.8

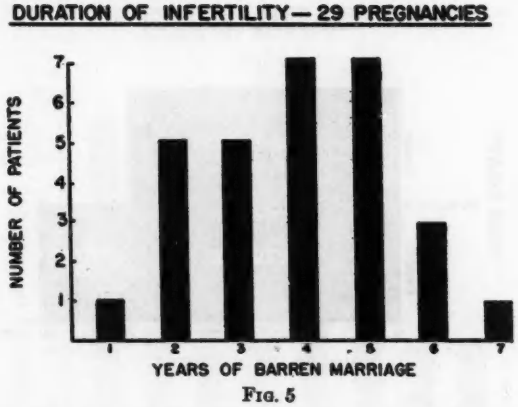

FIG. 5

sample of the particular ejaculate that hits the proverbial jackpot after years of failure. Despite the fact that these objections cannot be circumvented, the incidence of pregnancy is summarized in table 2. The wives of 29 (17.8 per cent) of our 163 patients became pregnant. No significant differences were noted between the groups with a) treatment, b) no treatment, c) high counts and d) low counts. Even the treated and untreated patients in the oligospermia group compared favorably (18.3 per cent and 18.2 per cent).

As seen in figure 5, the largest number of these 29 successful patients had been

stalked by failure for either 4 or 5 years. No pregnancies occurred after 7 years of barren marriage.

Medication in the 78 treated cases is summarized in table 3. The 4 drugs (thyroid, vitamin E, antuitrin S and testosterone) were given in practically every possible combination. The progynon case will be referred to later.

Although 14 pregnancies followed medication, only 5 of these occurred during the treatment (table 4). The other 9 patients had stopped all medication for 1 to 8 months before their successes. Further study of these cases failed to show any significant changes in motility or morphology. A few of the sperm counts improved, some actually decreased in number but most were unchanged while the patients were taking the medicines. The 14 successful patients in this treated

TABLE 3. *Medication in 78 cases*

DRUG	NO. OF PATIENTS*	DOSAGE
Thyroid	66	½–1 grain daily
Vitamin "E"	60	50–100 mgm. daily
Antuitrin "S"	12	1000–1500 u. weekly
Testosterone	8	30–60 mgm. (oral) / 25–50 mgm. (i.m.) weekly
Progynon	1	1500 r.u. per week

* Most patients eventually received more than one drug.

TABLE 4. *Pregnancies after medication*

TIME OF PREGNANCY	NO.	
After drugs stopped for		
1 month	3	
2 months	1	
3 months	1	9
4 months	2	
6 months	1	
8 months	1	
While taking vitamin "E"		3
While taking thyroid		1
While taking antuitrin "S"		1

group averaged 40,000,000 spermatozoa per cc at the time of the pregnancies but a few individuals were having counts as low as 3,000,000 per cubic centimeter at the time of the pregnancy.

Graphic summaries of some of these cases illustrate the unpredictable responses to medication. Figure 6, *A* shows improvement in motility and number followed by pregnancy while taking only vitamin E. Figure 6, *B* shows similar changes with the same result on thyroid extract.

Figure 7, *A* illustrates increase in number of sperm with pregnancy 2 months after simultaneous vitamin E and thyroid had been stopped, while 7, *B* shows pregnancy, despite the marked reduction in the count, during the same treatment.

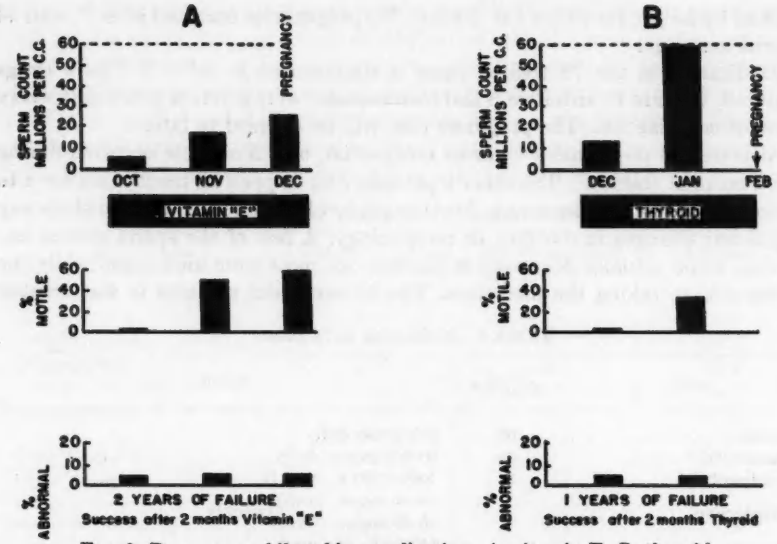

FIG. 6. Pregnancy while taking medication. *A*, vitamin E. *B*, thyroid.

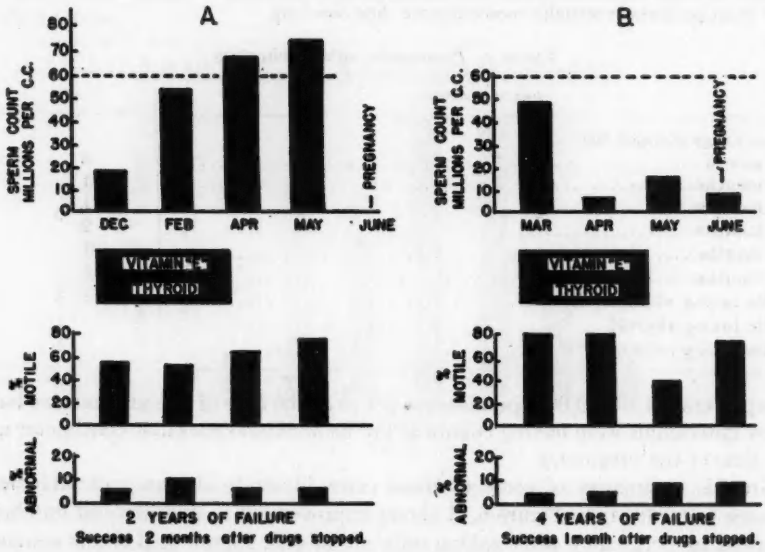

FIG. 7. Pregnancy after vitamin E and thyroid had been stopped. *A*, with increase in sperm count. *B*, despite decrease in count.

Figure 8, on the other hand, demonstrates the ineffectiveness of both drugs, even when given intermittently for 2 years.

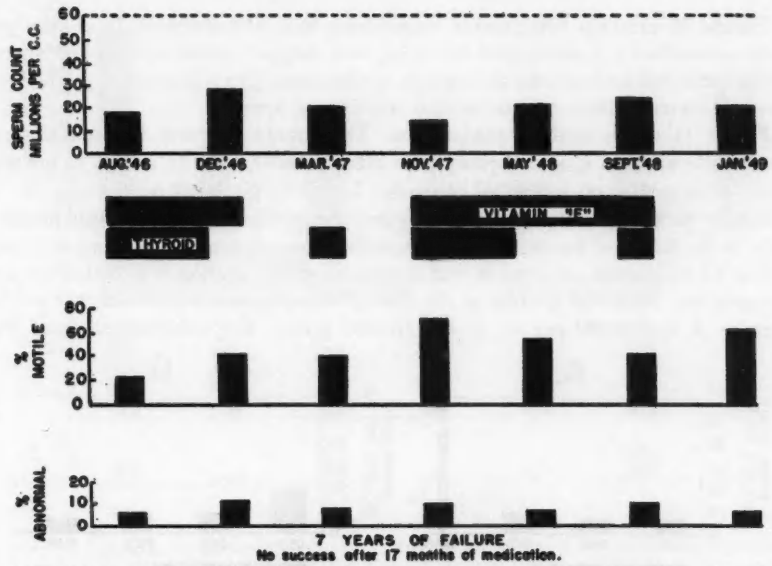

FIG. 8. Vitamin E and thyroid given intermittently for many months with no significant change.

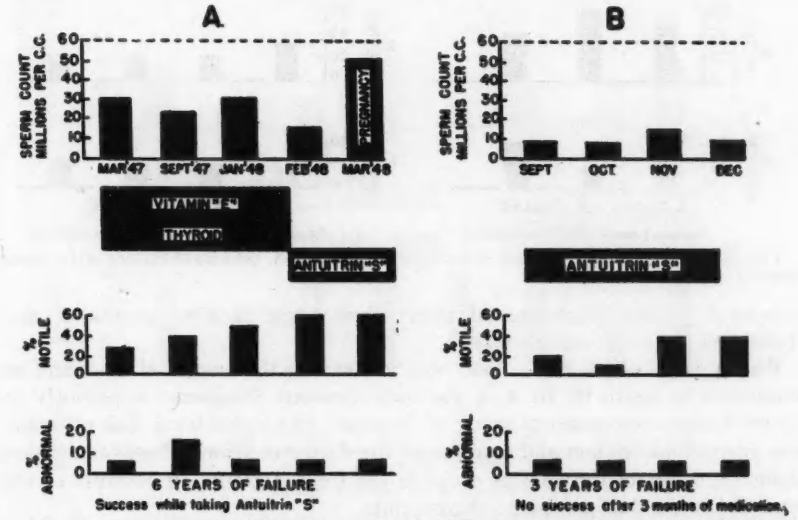

FIG. 9. *A*, pregnancy while taking antuitrin S. *B*, no change during antuitrin S.

Figure 9, *A* shows a similar failure, compensated for eventually during antuitrin "S" treatment. Figure 9, *B* illustrates the ineffectiveness of the same drug.

Figure 10 presents comparable experiences with testosterone. In *A*, the patient succeeded 1 month after the drug was stopped, even though the sperm count remained low and the percentage of abnormal forms increased. In *B*, there was continued failure and decreased number of sperm.

Figure 11 defies rational explanation. The counts dropped to an alarming level while vitamin E and thyroid were administered, only to return to normal range after progynon (estradiol benzoate) had been given by mistake.

Figure 12 shows failure of intensive and varied therapy over many months only to be followed by pregnancy 3 months after all medication was stopped.

The 15 successful patients in the untreated group averaged 80,000,000 spermatozoa per cubic centimeters at the time of the pregnancies, in contrast to the average of 40,000,000 per cc. in the treated group. Nevertheless, some of the

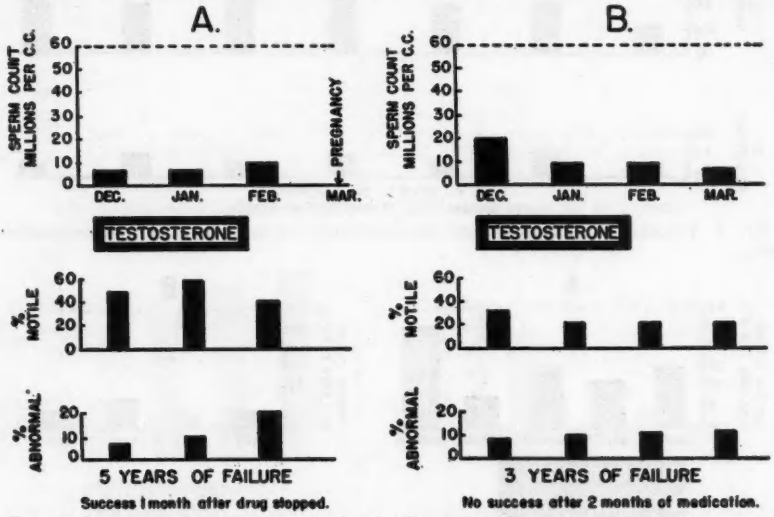

FIG. 10. *A*, success after testosterone despite low count. *B*, continued failure after testosterone.

untreated patients impregnated their wives while running counts of only 10,000,000 per cubic centimeters.

Two types of oligospermia were observed among the untreated cases and are illustrated by figure 13. In *A*, it was only transient. Pregnancy apparently occurred during a spontaneous swing of the count to a higher level. This phenomenon was not uncommon and emphasizes the danger of drawing hasty conclusions about the effect of the various drugs in the treated group. In contrast to this type, *B* is typical of persistent oligospermia.

Figure 14, *A* shows an untreated patient with normal counts whom we followed for 29 months with continued failure even though his wife has no pelvic abnormalities. *B* shows a similar but more fortunate individual who eventually impregnated his wife despite no medication.

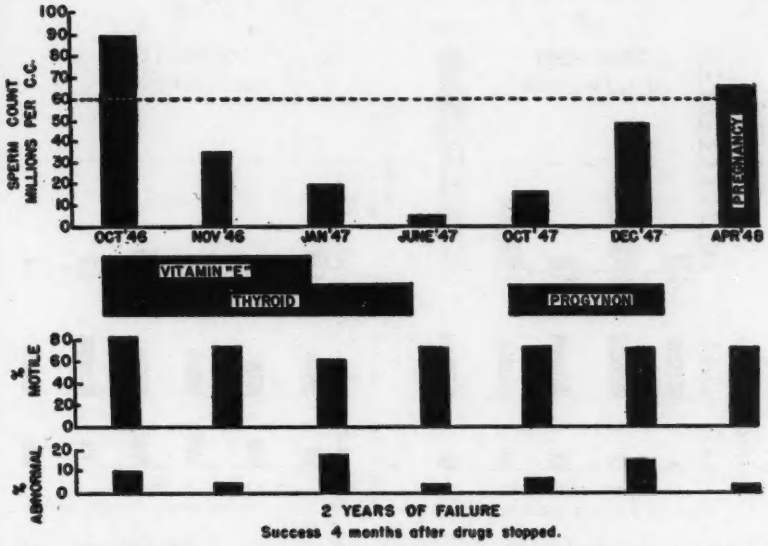

FIG. 11. Decrease in sperm count during vitamin E and thyroid with subsequent increase and pregnancy after estrogenic substance was given by mistake.

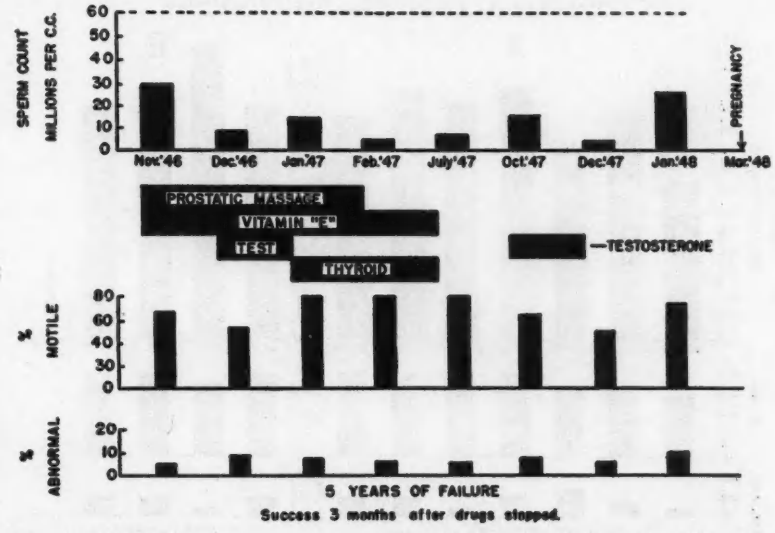

FIG. 12. Varied therapy over many months with pregnancy after all medication was stopped.

Very few conclusions are justifiable after a study of this type but a few observations cannot be ignored:

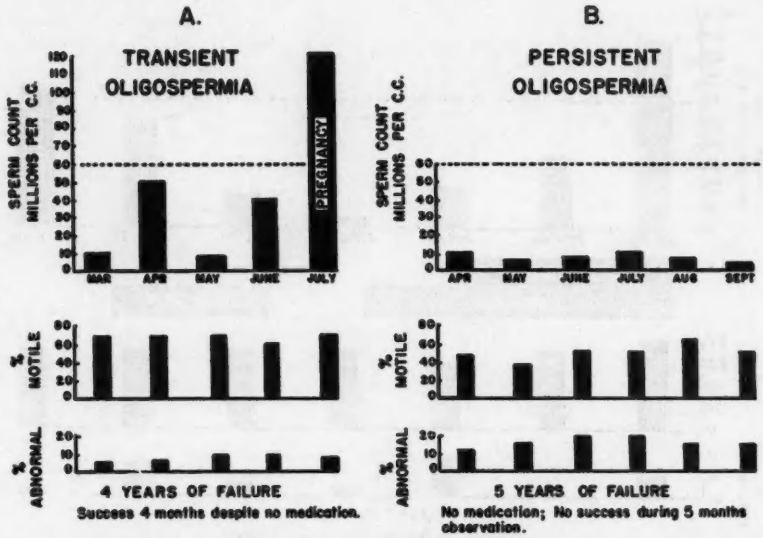

FIG. 13. Types of oligospermia. *A*, transient, with pregnancy during spontaneous swing to normal. *B*, persistent, with no significant fluctuations.

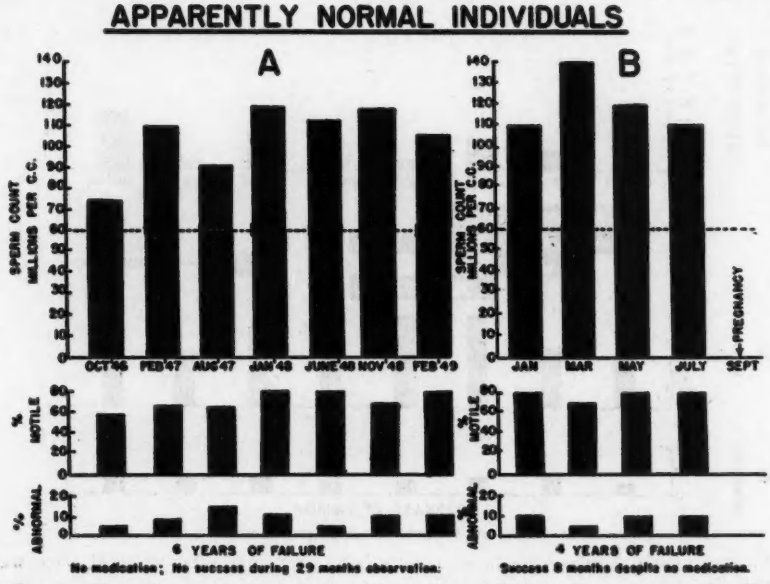

FIG. 14. Normal sperm pictures. *A*, with continued failure. *B*, pregnancy despite no treatment.

Motility and morphology of spermatozoa proved to be disappointing when one tried to account for decreased fertility.

Sperm counts gave the most significant data in this series of 200 males. Fifty per cent of the patients had oligospermia, 38 per cent had counts within normal limits and 12 per cent had azoospermia.

The incidence of pregnancy among 78 patients treated with vitamin E, thyroid, antuitrin S and/or testosterone was the same (17 per cent) as in a group of 85 patients who received no medicines.

Transient oligospermia, with spontaneous swings to normal, could explain most if not all of the favorable responses during or after medication. None of the 4 drugs tested had any consistent spermatogenic value. The psychic effect of such therapy is hard to evaluate.

Pregnancies were not dependent on high counts. Some occurred when the husbands were running 3,000,000 spermatozoa per cubic centimeter. The average for the 29 successful couples, however, was 60,000,000 per cubic centimeter.

Of 93 patients with frank oligospermia, 71 were treated and 22 were merely observed. Pregnancies occurred in 18 per cent of each group and were most unpredictable.

Many individuals with consistently normal sperm studies and excellent general health continued to be unable to impregnate their allegedly normal wives.

In this series barren marriages of more than 7 years' duration were not altered.

The following suggestions, therefore, are made for the busy practitioner who is plagued with male sterility problems and who cannot conveniently refer such patients to a large sterility clinic:

Limit the laboratory studies to carefully executed counts and only general observations about other sperm characteristics.

Delay specific classification of any patient until repeated counts are consistent over a period of several weeks.

Give medication only for its psychic or tonic value. A reliable spermatogenic drug is not available but the general health and peace of mind of any patient are most important.

Avoid prognoses, inasmuch as extreme oligospermia may be capable of causing pregnancy while normal counts may be accompanied by continued barren marriages.

DISCUSSION

DR. DAVID DAVIS (Philadelphia, Pa.): I hate to see Dr. Hamm's paper[1] go with so little comment. It is an excellent paper and an excellent effort, again, to try to rationalize our method of treating different cases of prostatic enlargement, and it was undertaken in a very rational spirit, which is more than can be said of some papers.

In further observation on this general problem, I would merely make two small suggestions which we have found somewhat useful: one, there is no doubt that cystoscopic observation before prostatic operations is important. However, it has occurred to us that there is no particular need for this cystoscopic observation to take place 24 hours or more before the operation, and therefore, along the line of minimizing infectious complications, we have made it a practice now for some years to perform the cystoscopic examination after the anesthetic is given, just before the operation. If unsuspected findings crop up at this moment, it is not at all too late to change the plan of attack, and in the great majority of cases, it does away with an reaction following preoperative cystoscopy and absolutely avoids any discomfort that might be associated with that procedure. We like the arrangement very much.

Second, in regard to the occasional appearance of Proteus vulgaris or other ammonia-forming types in these cases before or after operation, we should not forget that there is a very radical method of treatment of such infections, which, when the infection is confined to the bladder and urethra, is completely successful in a hundred per cent of cases. This method consists of the continuous administration of a slightly acid solution which, after it has been going successfully for 48 hours, will eliminate all Proteus completely and permanently.

This can be done in several different ways. If the patient is on urethral catheter drainage, it is possible to utilize it by means of a two-way catheter, and a very useful device in that connection is an ordinary Foley catheter from which the distensible bag has been removed. This gives a small channel for the inflow of the acid solution. The catheter, of course, must be held in place by adhesive plaster or some other device.

The criterion for success in this method is to have the outflow observed at very frequent intervals, making sure, with litmus and nitrazine paper, that it is always on the acid side. If it is kept constantly on the acid side for 48 hours, the Proteus will be gone. After operation, similar irrigations can be carried out, either through such a two-way catheter which goes in suprapubically, or if that is not easy, a very small catheter—let's say a No. 8 or No. 10—can be passed in through the urethra and used for the inflow of the acid solution. It must be a continuous drip, because injections even as frequently as every half-hour are are not sufficient to accomplish the desired result.

[1] Dr. Hamm has decided not to publish his paper at this time.

QUESTION: What acid do you use?

DR. DAVIS: Anything; it doesn't make any difference. Acetic acid, in strengths of ¼ or ½ of 1 per cent is excellent.

DR. WILLIAM J. ENGEL (Cleveland, Ohio): I would like to emphasize and lend support to Dr. Hamm's statement about the avoidance of the indwelling urethral catheter preoperatively in patients with prostatic obstruction.

For a long time I have felt that the indwelling urethral catheter was a dangerous instrument. Some years ago I called attention to the fact that not infrequently patients die before operation in whom the simple introduction of an indwelling catheter initiated the train of events leading to death. Infection with ascending pyelonephritis and uremia was the cause of death. Thus I have always tried to avoid the use of an indwelling catheter.

Dr. Hamm made the statement that the presence of a large residual urine is an indication for the use of an indwelling catheter. I question even that. I have brought here the x-ray film of a patient who had had pronounced obstructive urinary symptoms and who had been found to be carrying 800 cc or more of residual urine. He was admitted to the hospital, where blood studies were within normal limits, and an intravenous urogram was done. This is the No. 2 film taken 15 minutes after the injection of the dye. I call your attention to the normal kidney pelves. You will observe only the very slight dilatation of the lower ureters. The 5 minute film on this patient showed good excretion of the dye, which is an indication of satisfactory renal function.

When this patient arrived in the operating room the bladder was palpable two-thirds of the way to the umbilicus, but because of this normal urogram we had the courage to proceed with a one-stage suprapubic prostatectomy. The patient suffered no ill effects and proceeded with an entirely uneventful convalescence.

This is not an isolated case, but is presented as an outstanding example of one-stage prostatectomy in the presence of large residual urine. We routinely do intravenous pyelograms as part of the preoperative study of patients with prostatic obstruction. I believe one need not hesitate to do a prostatectomy in the presence of a relatively large residual urine provided the preliminary intravenous urogram reveals good renal function and there is no dilatation of the upper urinary tract.

The presence of residual urine alone does not, therefore, demand an indwelling catheter nor constitute a contraindication to doing a clean one-stage prostatectomy.

DR. HAMM (Closing discussion): I have nothing further to add, but I wish to thank the discussants.

DR. CULP (Closing discussion): We have followed Dr. Hotchkiss's text for the various sperm studies. We ask the patients to abstain from intercourse for at least three or four days, to avoid the use of condoms for collecting ejaculate, to use a wide-mouthed glass receptacle which we provide and on which we put an appropriate label. They are urged to present the specimen at the clinic as

soon after it is obtained as possible. It usually means that the wife has to hustle in with it.

We have designated an assistant resident who does all the sperm studies. He is thoroughly indoctrinated by his predecessor, and continues for 12 months. That is his sole duty on that day. It is this possible waste of man-hours which has us a little bit concerned as to what we are obligated to do so far as the patient is concerned.

The stains and so forth are such as Dr. Hotchkiss has outlined in his book. You will be able to follow those without any trouble.

ABACTERIAL PYURIA, ACUTE AND CHRONIC: ITS PROGRESS AND TREATMENT

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Infectious abacterial pyuria has been brought to the attention of the urologists of this country during the second great war. The current literature on this subject has been ably summarized by Briggs in 1935 and Moore in 1943, and for this reason no long historical survey will be included in this publication. Sterile pyuria has been described since 1909 and was classified as a distinct entity in 1921 being determined "true infectious amicrobic pyuria." In 1916, Reiter first described a clinical syndrome characterized by urethritis, conjunctivitis and arthritis, while in 1933, Wildbolz first advocated neosalvarsan as specific treatment.

The literature describing both Reiter's disease and abacterial pyuria has recently recorded many more cases, but certain aspects of the disease have not been emphasized. It is the purpose of this communication to discuss the disease of abacterial pyuria in two phases: 1) the acute; and 2) chronic.

1. ACUTE ABACTERIAL PYURIA

This is a clinical entity typified by the sudden onset of scant to profuse purulent urethral discharge with or without a history of recent exposure, followed in a varying time interval by intractable day and night frequency and severe dysuria. Terminal gross hematuria or even frank total gross hematuria occurs associated with slight pyrexia. The white blood count varies between 10 to 20 thousand. The sedimentation rate is usually rapid. The striking feature of the disease is the absence of any of the common organisms in the urine, which contains many pus cells and red blood cells. Urinalysis is negative for M. tuberculosis.

In a fairly high percentage of cases, intravenous urography done within 3 weeks to 4 months of the onset of the disease, reveals dilated kidney pelves and dilated ureters extending down to a small spastic, irregular bladder. The extreme lower ends of the ureters are often observed as thin thread-like lines in the area of the ureterovesical junction.

Cystoscopic examination of these patients is extremely difficult, even under spinal anesthesia, due to the small capacity of the bladder. The typical appearance has been described in the literature. It is one of widespread edema and areas of superficial ulceration scattered throughout the whole bladder.

Three cases of acute abacterial pyuria illustrating the above points have been treated by means of intravenous arsenical compounds. A detailed case report of one of these cases is presented for illustration and to demonstrate the results of treatment.

Case report. H. T., admitted January 18, 1947, was a 45 year old white man in perfectly good health until 11 weeks prior to admission. At that time, without any history of ex-marital contact, he developed a purulent urethral discharge. Cultures taken at this time were negative for gonococci.

Ten weeks before admission he developed urinary frequency up to 20 times throughout the day and 6 times at night. He was treated for 3 weeks with adequate dosage of sulfathiazole with no relief from any symptoms. He was then treated for 2 weeks with 150,000 units of penicillin daily in divided doses with no relief.

Two weeks following penicillin there was some improvement in his symptoms of frequency, but within a further week the frequency had recurred and was now q.15 to 30 minutes day and night.

FIG. 1. Acute abacterial pyuria. *A*, 30 minute intravenous urogram, before treatment. *B*, 30 minute intravenous urogram after 4 intravenous injections of arsenic on alternate days. *C*, 30 minute intravenous urogram 2 weeks after initiating arsenical therapy.

During the above period of approximately 9 weeks he had received, in addition to sulfathiazole and penicillin, adequate treatment for prostatic infection in the form of Sitz baths, prostatic massage, silver nitrate instillations.

He was referred 11 weeks from the onset of his complaints because of the failure to relieve his symptoms.

A physical examination revealed slight but definite evidence of weight loss but was otherwise negative.

Laboratory studies: Nonprotein nitrogen 49 mg., hemoglobin 100 per cent, sedimentation rate 80 mm. The urine was slightly blood stained, acid in reaction, specific gravity 1.023. Microscopic examination of the urine after destroying the red cells revealed 200 to 300 pus cells per high power field uncentrifuged. The culture of the urine taken by catheter failed to grow any of the common organisms. It was likewise negative for M. tuberculosis.

Cystoscopic examination revealed a bladder capacity of 1 ounce with a markedly reddened, edematous mucous membrane and several areas of superficial ulceration. Intravenous urography disclosed marked bilateral hydronephrosis and hydro-ureter with a small contracted bladder (fig. 1, *A*).

A diagnosis of acute abacterial pyuria was made and on the third day of his hospital admission he was given mapharsen .04 gm. intravenously. This drug was repeated in doses of .06 gm. on alternate days for 6 doses. No other treatment was given.

Within a period of 10 days his symptoms had entirely disappeared. The frequency was now D/N = 5/0–1. There were occasional pus cells in the urine, which on culture remained sterile. An intravenous urogram revealed a normal sized bladder with slight degree of hydronephrosis and hydro-ureter, as well as a fine thread-like appearance at the extreme lower end of the ureters.

During the following 9 days the patient was completely asymptomatic, the frequency D/N = 3–4/0, the urine microscopically negative and the culture still sterile.

Intravenous urography 19 days from the beginning of treatment revealed normal kidney pelves and ureters except for the extreme lower end of the left ureter (fig. 1, *C*). The bladder was normal.

The patient was discharged from hospital and has been closely followed since that time. There has been no symptomatic recurrence.

2. CHRONIC OR SUBACUTE ABACTERIAL PYURIA

The acute phase of this disease has been stated by some writers to be self-limiting, regardless of the type or efficiency of treatment. Other authors believe it to be self-limiting, but with marked tendency to recurrence. Since 1945, 5 patients have been referred to our center, from other institutions, presenting great problems in diagnosis and treatment.

In all cases there was widespread dilatation of the ureters and kidney pelves with a small contracted bladder. Complete investigation repeated on many occasions failed to show any evidence of the common bacteria. Repeated cultures and guinea pig inoculations were also done for M. tuberculosis; these were negative. Penicillin, sulfathiazole and sulfadiazine in large doses had had no effect upon the course of the disease. The usual procedures in the treatment of lower genito-urinary tract infection had been ineffective. Four of these 5 cases had been complicated by the appearance of multiple joint lesions associated with conjunctivitis rendering the case rather typical of so-called Reiter's disease.

Because of these findings it was postulated that the patients suffered from abacterial pyuria. They were, therefore, subjected to repeated courses of mapharsen, consisting of .06 gm. every third day for 6 doses. There was no clinical improvement. The mapharsen was repeated on alternate days in doses of .045 gm. for 2 weeks, again without improvement.

Following the use of mapharsen a rest period of 3 weeks to a month was instituted and the patients were then given a course of neosalvarsan. This arsenical compound also failed to produce any symptomatic relief.

Intravenous urography was repeated each month over a period of time while these patients remained in hospital. These various examinations showed a gradual but constant increase in the hydronephrosis and hydro-ureter associated with a slow, steady, decrease in kidney function as demonstrated by the administration of uroselectan (fig. 2). There were irregular, repeated, exacerbations of the joint

disease, associated with increased frequency and gross hematuria indicating that there had been no limitation of the disease.

Because of the marked similarity and the length of history in these cases only one case history is presented for illustration of this progressive type of lesion.

Case report. E. C., admitted May 31, 1944, was a 19 year old white man who had been in previous good health until 3 weeks prior to admission, when he developed a urethral discharge following exposure 7 days previously. Smears and culture at the onset of urethral discharge failed to reveal gonococci. Two days following the onset of urethritis there was marked frequency day and night with dysuria. These symptoms were followed in a further 4 days by intermittent gross hematuria.

Fifteen days after the onset of urethral discharge, there was swelling and redness with severe pain in the right wrist, right shoulder and left knee. At this time, in spite of negative smears and cultures, he was considered to be suffering

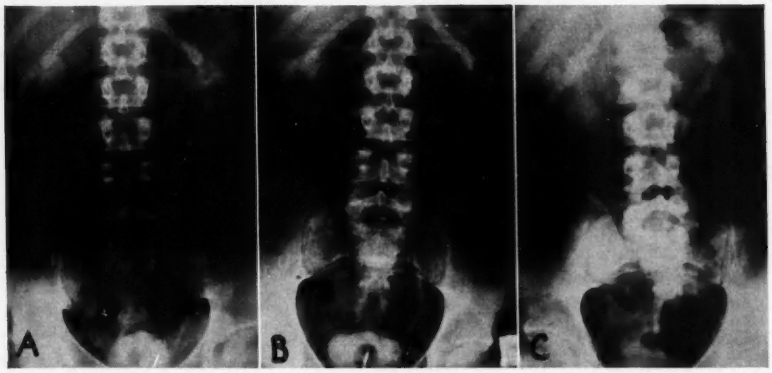

FIG. 2. Chronic abacterial pyuria. *A*, 30 minute intravenous urogram taken July 31, 1946. *B*, 30 minute intravenous urogram taken August 29, 1946. *C*, 75 minute intravenous urogram taken November 27, 1946. There was no demonstrable function up to 60 minute interval.

from acute gonorrheal urethritis and arthritis and was accordingly transferred from his military unit to a field hospital. He was treated by the intramuscular administration of 500,000 units of penicillin over a 3 day period. There was no change in the clinical signs and symptoms. At this time the gonorrheal fixation test was reported as negative and remained negative on further repeated examinations.

At this time he began to complain of swelling and redness of his left eye. On examination this was diagnosed as subacute conjunctivitis and smears taken from the conjunctival sack were again recorded as negative for gonococci.

Over the period of the following 2 months, the patient was confined to the field hospital. There was slight improvement in the joint symptoms following the administration of salicylates, but his urinary symptoms of frequency, dysuria and intermittent hematuria persisted. During this period repeated urinalysis showed many pus cells, but at no time were urine cultures made.

Two months following his admission to the field hospital an intravenous urogram showed bilateral hydronephrosis with dilatation of both ureters throughout their entire length. There was a small spastic bladder.

Three months from the onset of his illness he was transferred to a permanent hospital under the care of an urologist.

The urine was loaded with pus and an occasional red blood cell. The prostatic smear showed 100–150 pus cells and the two-glass urine was recorded as cloudy in both glasses. The sedimentation rate was 94 mm., with elevation of temperature to 99½ F. There was no evidence of acute arthritis, the eye lesions had healed, and the diagnosis at this time was considered to be prostatitis, possibly gonorrheal in origin.

For this reason the patient was subjected to 3½ hours of fever therapy, as well as regular prostatic massage. It was considered that his condition was improving although no symptomatic relief from the frequency and dysuria had been obtained. At the end of 8 months' hospitalization, he was returned to his unit.

He was re-admitted to hospital early in 1945, with severe frequency and dysuria and occasional pain and swelling of the right shoulder, wrist and left knee. There was also a history of intermittent gross hematuria since discharge from hospital. He was again treated by sulfadiazine and penicillin with little or no change in symptoms. The urine was recorded as loaded with pus and red blood cells but again no culture was obtained. The patient was discharged only to be re-admitted several times throughout 1945, and the early part of 1946. In October 1946, the patient was referred to the author's service, at which time his complaints were still frequency every hour, day and night, with occasional gross hematuria lasting 1 to 2 days, usually associated with some discomfort in the joints of his right arm and left leg. The urine was loaded with pus and red blood cells and sterile on ordinary culture medium. Special cultures for tuberculosis were later reported as negative. The prostate was slightly enlarged, the prostatic secretion showed 100–150 pus cells and was sterile on culture.

Intravenous urography revealed moderate hydronephrosis on the right side, with a dilated right ureter (fig. 3, *A*). The left kidney showed some minor degree of hydronephrosis with slight dilatation of the ureter. The bladder was small and spastic. Cystoscopy showed the bladder capacity to be 2 ounces. The mucosa was diffusely inflamed with two or three small areas of superficial ulceration at various points throughout the bladder. Cultures taken from both kidneys showed no pus cells and were sterile on culture. They were also negative for tuberculosis. The nonprotein nitrogen was 32 mg. per cent.

In view of the history and the positive findings, a tentative diagnosis of abacterial pyuria was made and the patient given an extensive course of mapharsen therapy. There was no change in his clinical condition. He was, therefore, given a rest period of 1 month and treated with large doses of neoarsophenamine with no improvement.

An intravenous urogram showed little change from the films taken 1 month previously. In view of the persistence of urinary symptoms, in spite of all types of treatment over a period of 2½ years, and the presence of a static or slowly in-

creasing hydronephrosis and hydro-ureter associated with a small spastic bladder, we advised the patient to submit to uretero-intestinal anastomosis.

This operation was performed in January 1947. Portions of the ureter were removed for microscopic study. These showed no evidence of tuberculosis, but did show widespread chronic inflammatory changes with marked edema of the ureteral wall (fig. 4). His postoperative course was uneventful and his symptoms of frequency and dysuria were entirely relieved.

Repeated pyelographic studies since that time have shown an increasing hydronephrosis and hydro-ureter with decreasing kidney function. However, the patient has been constantly employed as full time waiter in a large hotel since March of 1947.

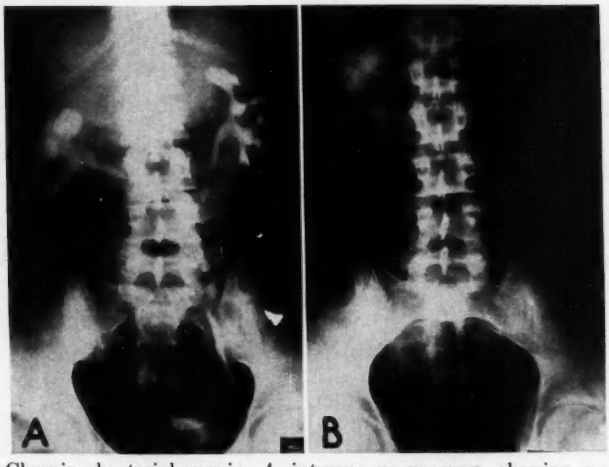

FIG. 3. Chronic abacterial pyuria. *A*, intravenous urogram, showing moderate right hydronephrosis and hydro-ureter with slight pathological changes on left side. *B*, upper urinary tract 5 months following Coffey transplant; compare with *A*.

TREATMENT

Due to the severe and constant urinary frequency, these patients were unable to sleep or to maintain adequate nutrition. This fact, combined with the steady decrease in kidney function and repeated exacerbations of symptoms, following years of what we considered to be adequate conservative treatment, persuaded us to attempt surgical procedure designed to overcome the obstruction at the ureterovesical junction.

Four patients were therefore subjected to bilateral uretero-intestinal transplantation. Three patients were transplanted by the method Coffey 1, while the fourth patient was operated upon using the method of direct elliptical suture. In all cases there was total relief of their intractable frequency, nutrition was improved and a definite gain in weight occurred. The patients were able to leave hospital and resume their occupations, but have not been able to do hard manual labour.

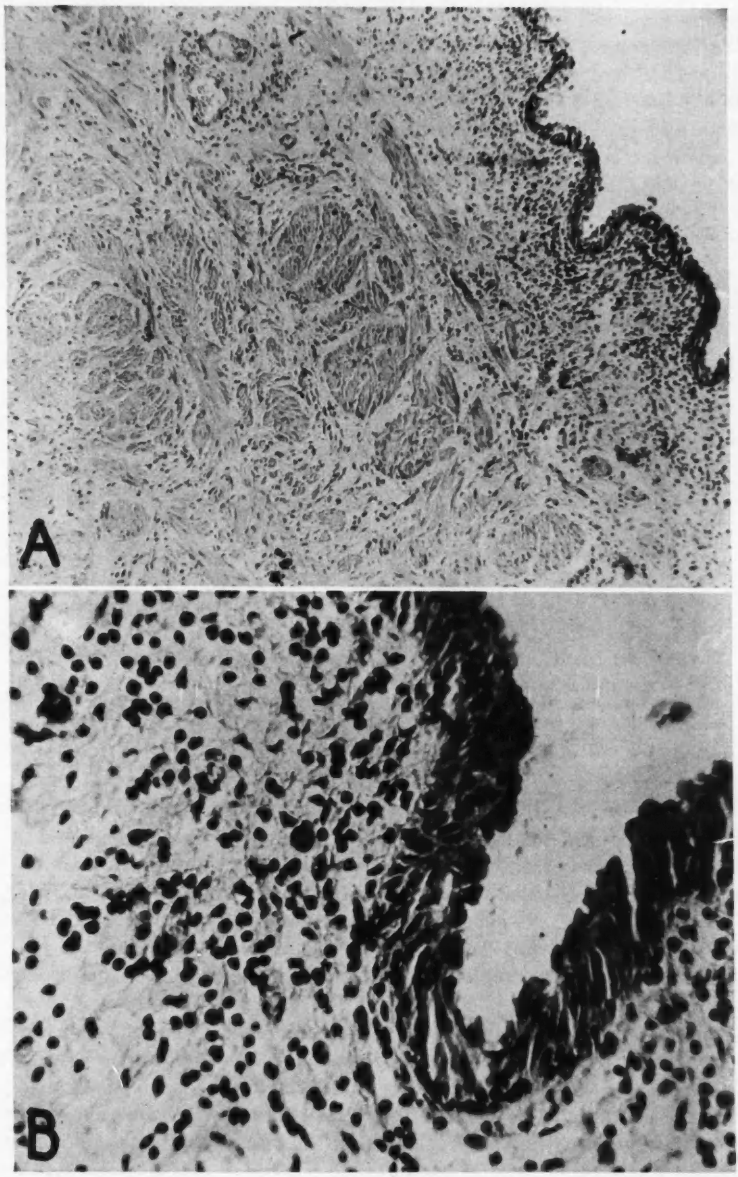

FIG. 4. Chronic abacterial pyuria. *A*, low power view of ureteral section, showing marked edema and chronic inflammatory change. There is no evidence of tuberculosis. *B*, high power view of *A*.

As has been our experience in a high percentage of the Coffey type transplantation done for other diseases there was no decrease in the size of the hydronephrosis and hydro-ureter, but rather there was a definite increase in both these factors (fig. 4, *B*). The one case transplanted by elliptical anastomosis showed a definite decrease in hydronephrosis and hydro-ureter thereby conforming with our experience in this operative procedure for the treatment of carcinoma of the bladder (fig. 5).

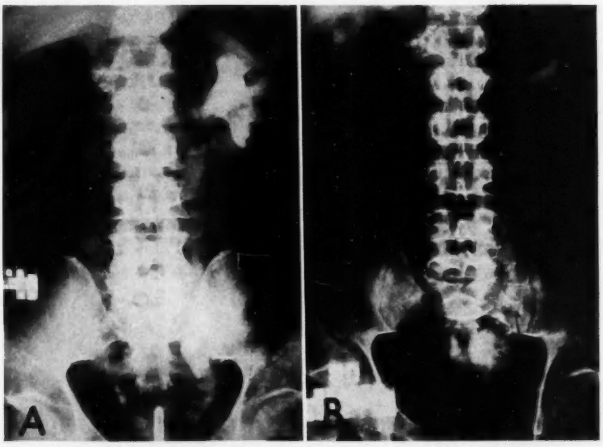

FIG. 5. *A*, preoperative intravenous urogram of chronic abacterial pyuria, showing marked hydro-ureter and hydronephrosis. *B*, postoperative intravenous urogram following elliptical anastomosis; note decrease in hydronephrosis.

SUMMARY

We have presented 3 similar cases of acute abacterial pyuria utilizing the details of 1 case for demonstration purposes. These cases were diagnosed in the acute stage and were treated by a specific therapy, namely mapharsen. The evidence of pathological lesions in the upper genito-urinary tract disappeared in a very short period of time, no longer than 10 days to 2 weeks. This disappearance was co-incidental with a rapid and marked increase in the bladder capacity associated with complete disappearance of the patients' signs and symptoms.

We have presented one detailed case as illustrative of a group of patients whom we believe suffer from the same clinical disease, but in whom, because of the lack of early diagnosis and adequate treatment, the disease has been progressive and exhibits the characteristics of Reiter's disease. We have been unable to relieve the symptoms, or to arrest the progression of the disease, by the use of any antibiotics or by any other type of conservative treatment. Four of these patients have been subjected to uretero-intestinal transplantation with marked symptomatic improvement.

CONCLUSIONS

Abacterial pyuria in its acute phase is often associated with dilatation of the upper urinary tract.

Acute abacterial pyuria is cured, with the disappearance of all signs and symptoms within 1 to 2 weeks, by the administration of arsenicals. In this group we have used mapharsen.

This is not a self-limiting disease in all cases and the progressive case accurately resembles the clinical picture of Reiter's disease. Abacterial pyuria and Reiter's disease are therefore probably different manifestations of the same clinical condition.

Bilateral uretero-intestinal transplantation has been performed in 4 cases. There has been relief of symptoms in all patients, but in those treated by the Coffey 1 method of transplantation there has been no improvement in the upper urinary tract lesions. The one case treated by direct elliptical anastomosis has shown definite anatomical improvement in the kidney and ureter.

It is necessary and essential that the diagnosis should be made and adequate treatment instigated in the acute phase of abacterial pyuria.

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INSTRUMENTAL VISUALIZATION OF THE RENAL PELVIS AT OPERATION AS AN AID TO DIAGNOSIS. PRESENTATION OF A NEW INSTRUMENT

W. F. LEADBETTER

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Five years ago while the author was in North Africa as urologist with an army general hospital, numerous patients with renal and ureteral calculi were treated. Some of them had multiple small renal calculi visualized by x-ray which were assumed to be attached to the surfaces of renal papillae (Randall's disease). At operation on several occasions for the removal of a calculus obstructing the ureteropelvic junction, it was impracticable to attempt removal of tiny calculi in calyces. It occurred to us that it would be interesting and technically possible to construct an instrument which would allow visualization in situ of calculi so situated. Also, it was believed that such an instrument used more or less routinely in stone cases at operation might anticipate the recurrence of calculi by demonstrating early plaques on renal papillae. The possibility of attaching a small forceps to such an instrument was considered which would allow small adherent calculi to be torn away from a papilla without the difficulty and trauma inherent in an open surgical attack. Another possible application of such an instrument was the visualization of small lesions in pelvis, infundibula, and calyces such as hemangiomas or tumors responsible for hematuria which may not be diagnosed with certainty by pyelography or even exploration at operation. It was believed that conservative surgery for some of these lesions was possible if their exact nature and location could be established, thus avoiding nephrectomy which otherwise becomes the only recourse.

With the end of the war and return to civilian practice, Mr. Frederick Wallace of the American Cystoscope Makers, Inc. was consulted and the problem explained. A basic pattern for such an instrument was suggested. He expressed interest and agreed to make the instrument. After 2 years' delay, the instrument was completed and given to me at the 1948 meeting of the American Urological Association.

At that meeting Dr. Trattner presented his instruments and experience in their use. He utilizes a straight 24 F sheath with three different telescopes: observation, operating, and catheterization (for catheterization of infundibula). Lens views are forward, foroblique and right angle as in the Vest, McCarthy, and Brown-Buerger instruments, respectively. It would appear that certain limitations are inherent in the use of a straight sheath. Even though the kidney is completely mobilized, visualization of the ramifications of the pelvis (infundibula and calyces) will be difficult if not impossible, and only occasionally in the

normal kidney can papillae be studied in detail. This technical limitation prompts me to present the instrument which I have been using, since I believe, to some extent, it extends our present diagnostic abilities.

The instrument is much simpler and as yet is not fitted with operating attachments so that its use is restricted to inspection of the renal pelvis, infundibula, and calyces. Its use, however, has been rather satisfactory so that it seems worth while presenting it in its as yet uncompleted state

The instrument consists of a single unit (fig. 1). The long shaft contains a telescope, conduits for electric current, water, and a small accessory channel which may be used either for the return of irrigating fluid or through which a steel guide-wire may be passed to perforate the renal cortex and localize a lesion for the purpose of direct operative exploration or treatment. The working end of the instrument is a 2½ inch arm placed at a right angle with the shaft. It terminates in a light socket, forward vision lens and open tubes. The instrument is

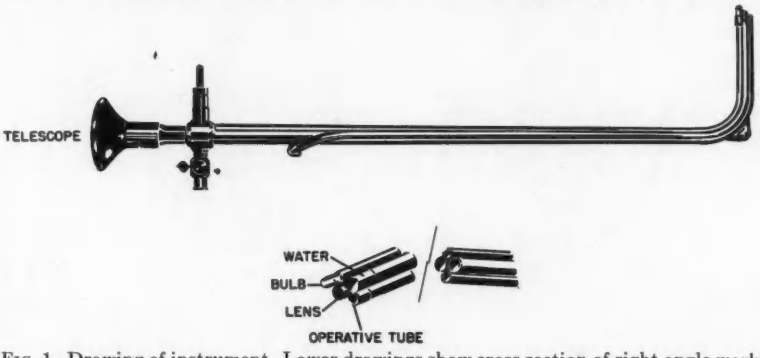

FIG. 1. Drawing of instrument. Lower drawings show cross section of right angle working arm and tip of instrument.

size 22 F which allows it to enter infundibula and most calyces with comparative ease.

At operation the kidney is exposed and mobilized completely. A small pyelotomy incision is made either on the anterior or posterior surface of the pelvis through which the instrument is carefully inserted. No effort to place a purse-string suture about the pyelotomy incision to prevent leakage of irrigating fluid is made, but the wound is carefully packed off with pads. Inspection of the pelvis, infundibula, and calyces is carried out, meanwhile allowing normal saline or sterile water to enter the pelvis from an irrigating flask at low pressure through the irrigating channel and sucking it out of the opening in the pelvis as it appears. In this way, a very clear view of the pelvis is obtained without trauma or stirring up bleeding. There seems to be no particular contra-indication to the procedure unless tuberculosis or papillary tumor is present. One would hardly conceive of the need for carrying out such a procedure in the presence of tuberculosis, and in the second instance the advantages may considerably overshadow the possibility of implanting cells. If the wound is properly packed off and the return

fluid sucked out by an assistant as it drains from the pelvis, little danger of cells being implanted seems likely.

The technical difficulties of studying the pelvis, infundibula, and calyces are not great for one skilled at cystoscopy. Figure 2 illustrates the manner in which the instrument may be used. The pelvic surfaces are clearly visualized by sweeping the instrument across the anterior and posterior walls and the ureteropelvic junction may be visualized and catheterized. The opening of infundibula may be located and studied and the end of the instrument insinuated into an in-

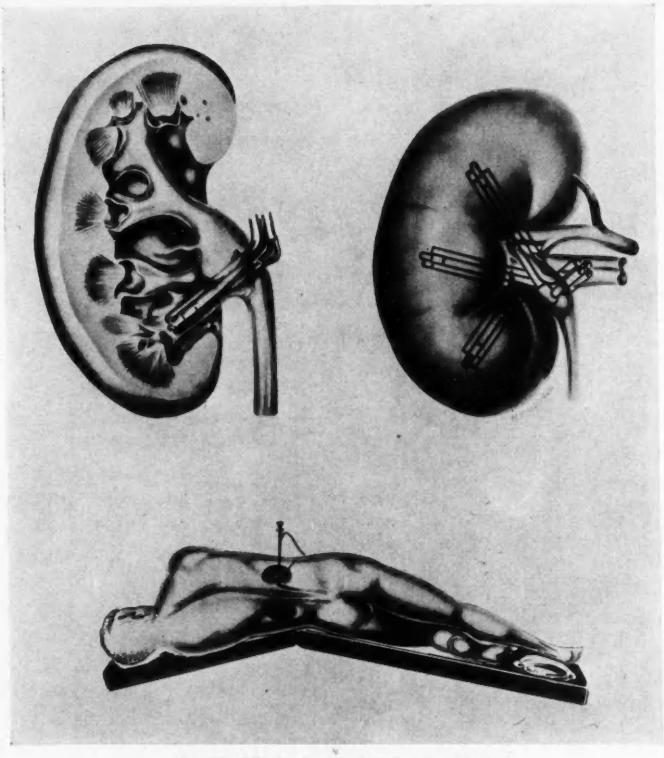

FIG. 2. Method of using instrument.

fundibulum. By slight molding of the kidney and pressure on the instrument, it may be slipped up to the calyces. Renal papillae may be seen with clarity. We are not sure how many of the calyces in the normal kidney may be visualized. We have seen many of the superior, middle, and inferior calyces and papillae. Individual variations as to numbers of calyces relative to infundibula and size of passages are the limiting factors. In the case of a slightly hydronephrotic or markedly hydronephrotic kidney, all calyces and papillae may be visualized with ease. A good stereoscopic retrograde pyelogram should be obtained and studied

prior to instrumental examination of the pelvis, because it gives the examiner a spatial conception of the infundibular and calyceal arrangement. The pyelogram should be on view to guide the examination.

The right angle shaft makes it possible to enter upper, middle, or lower calyces without the necessity of assuming a strained position or contaminating the wound, since the ocular end of the instrument may be rotated, moved up, down, or from side to side in a relatively short range and still give the working end almost any desired position. Gloves should be changed after the instrumental examination before proceeding with surgery.

The potential value of such an instrument is illustrated by the following case.

CASE REPORT

A 32-year old veteran admitted to the West Roxbury Veterans Hospital on July 7, 1948, complained of bloody urine. He first noted "dark" urine some time in 1945 while in the army. There was no history of previous urinary troubles. Several months following discharge from the army he applied for civilian insurance and was refused because of red blood cells found in the urine on several occasions. The patient did nothing about this. About 1 year prior to admission he began to notice gross blood in his urine and this had continued with short periods of remission until his admission. For several days before coming to the hospital, small clots were passed in the urine, and the morning of the day before admission he was awakened from sleep with dull pain in the left side which radiated to the groin and testicle. The past and family history was negative.

Physical examination revealed a well developed, well nourished man. Temperature, pulse, and respiration were normal. Heart and lungs were negative. Palpation of the abdomen revealed tenderness in the left upper quadrant and flank. No mass could be felt. External genitalia were normal and the prostate and vesicles were normal.

The urine was grossly bloody. Blood studies showed no abnormalities other than mild anemia. No calcified shadows were visualized in a plain x-ray of the abdomen. An intravenous urogram failed to demonstrate function on the left side. There was diminished function on the right. The nonprotein nitrogen was 67 mg. per cent. Cystoscopy revealed a normal bladder. Blood was seen coming from the left ureter; none from the right. Both ureters were catheterized and pyelograms obtained. These showed a small right kidney with slightly dilated calyces and evident loss of cortex (fig. 3, *A*). On the left side the pelvis failed to fill well. The pyelogram suggested filling defect due to a blood clot or tumor (fig. 3, *B*). Urine from both kidneys was sterile and negative for tubercle bacilli. A severe febrile reaction took place after cystoscopy and the urine culture grew Aerobacter aerogenes. Several days later a large amount of blood clot was passed and following this fever and pain subsided promptly. Subsequent cystoscopy was carried out and a left retrograde pyelogram (fig. 3, *C*) obtained which showed some dilatation of the pelvis and calyces. A definite diagnosis was not possible. The patient was discharged to be followed in the out-patient department. No gross blood was present in the urine at the time of discharge.

The patient failed to report until November 17, 1948, when he stated that he had been bleeding almost continuously since his discharge in the summer. He felt weak and tired, but had been working in spite of this.

Examination revealed no change in his general physical state. The hemoglobin was 54 per cent. The white blood count was 10,900. The nonprotein nitrogen was 24 mg. per cent. Hinton and Kahn tests were negative. The urine culture

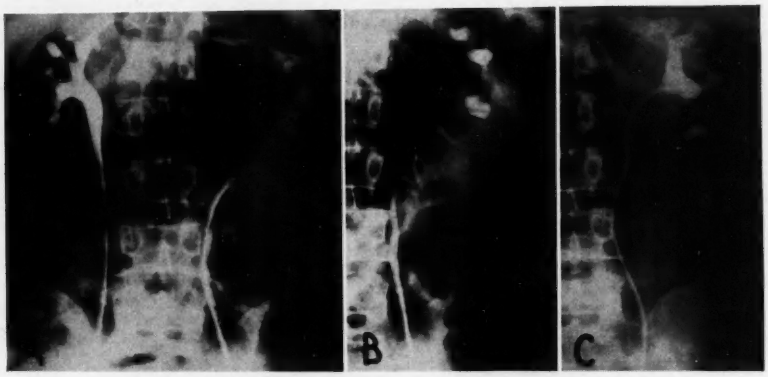

FIG. 3. *A*, right retrograde pyelogram. Outline of kidney cannot be seen, but cortex is thin. *B*, left retrograde pyelogram, showing filling about blood clot in upper ureter and pelvis. *C*, left retrograde pyelogram before discharge at time of first admission. Calyces still dilated, but no filling defect is visualized.

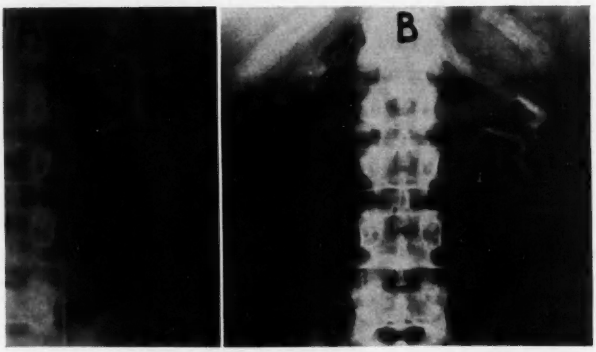

FIG. 4. *A*, left retrograde pyelogram at second admission. Pyelogram appears normal. *B*, postoperative intravenous urogram, showing small, poorly functioning right and left kidney with distortion of upper infundibulum and calyces.

was sterile. The urine was grossly bloody. It was negative for sugar. The specific gravity was 1.011.

The patient was transfused and 2 days after admission cystoscopy was done and retrograde pyelograms made (fig. 4, *A*). The left pyelogram appeared normal at this time and stereoscopic films failed to reveal anything except a possible small filling defect in relation to the upper calyx. Over the next week irrigations

of the left renal pelvis with silver nitrate solution in increasing strengths was used without any change in the degree of hematuria.

Finally, in view of the fact that the right kidney was atrophic and incapable of supporting life, the left kidney was explored in the hope that visualization of the interior of the pelvis and calyces would allow us to determine the cause of the bleeding and stop it.

At operation the left kidney was completely mobilized and found to be normal in external appearance. A small pyelotomy incision was made in the medial surface of the pelvis and the instrument carefully inserted. Inspection of the pelvis showed a normal mucous membrane. The openings of the superior, middle, and inferior infundibula were located with ease.

The upper infundibulum was entered and the instrument was slipped up this until the calyces were seen. Two upper pyramids could be plainly visualized in close detail. The most superior pyramid looked abnormal. It was flattened, irregu-

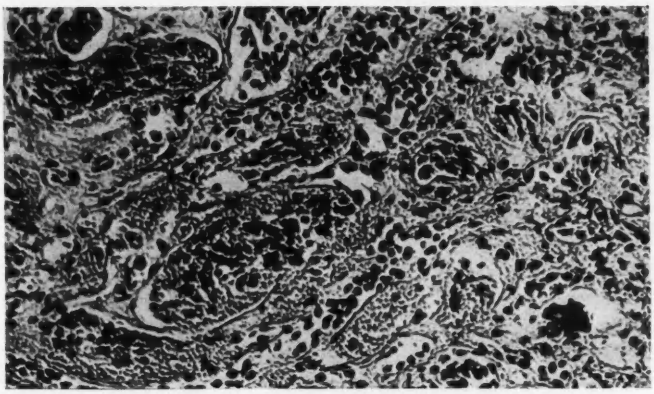

FIG. 5. Photomicrograph, showing excised papilla with distortion and scarring.

lar, inflamed, and at several points were small polypoid projections or granulations. The other superior pyramid appeared conical, smooth, and healthy. One superior calyx could not be directly visualized. In the pyelogram it will be seen that this enters the pelvis from a lateral and somewhat inferior direction. The mid calyx and lower calyces were studied and found to be normal in appearance.

It was decided that we were dealing with some sort of a lesion involving the superior calyx and that we would make a nephrotomy incision through the upper pole and try to decide whether we were dealing with a tumor or other lesion.

An incision was made, exposing the upper calyx and pyramid which looked scarred at the tip and felt firmer than normal. The papilla was excised and a nephrostomy tube introduced into the pelvis through the upper calyx. No effort was made to excise the cortical tissue which appeared normal.

The postoperative course was satisfactory. Bleeding stopped 2 or 3 days later and did not recur after removal of the nephrostomy tube 2 weeks after operation. The wound healed promptly. Intravenous pyelograms 20 days after operation

showed good function from the kidney. There was some distortion of the upper infundibulum with absence of the superior calyx (fig. 4, *B*).

Aside from one episode of hematuria which occurred in February of this year and cleared after 2 days, the patient has been asymptomatic. He has been working steadily. A telephone conversation on April 17 confirmed this.

Pathological report: "The specimen is a piece of soft, granular, pink and gray tissue measuring 4 by 8 by 1 mm. Microscopic examination reveals a distorted picture which appeared to be renal pyramid. There is no pelvic epithelium but considerable extraneous fibrous tissue. No evidence of tumor or tuberculosis." Diagnosis: Poorly preserved renal pyramid with chronic inflammation and scarring (fig. 5).

COMMENT

In the absence of any history of urinary symptoms in the past, sterile urine on the first examination, and our failure to demonstrate tubercle bacilli, it is difficult, if not impossible, to make a real diagnosis in this case. The contraction of the right kidney with marked impairment of function and absence of obstruction anywhere along the ureter does suggest previous severe infection of this kidney. The pyelogram certainly does not suggest the usual congenital hypoplastic kidney. It would appear that we were dealing, in the left kidney, with a localized papillitis involving the upper calyx due to disease which caused much local damage and which failed to heal properly. The possibility of some peculiar virus infection or toxic process must be considered.

CONCLUSIONS

An instrument is presented which allows easy visualization of the renal pelvis, infundibula, and many calyces after introduction through a small pyelotomy incision at open operation.

The technique of its use is discussed.

A case is presented which demonstrates the value of such an instrument.

After direct study of the pelvis, infundibula, and calyces, a nephrotomy incision was made and an abnormal papilla noted at pyeloscopy excised. This showed a chronic inflammatory process with scarring.

To date, 5 months after operation, the patient is well, whereas almost constant hematuria had been present for 2 years prior to operation.

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TRANSMIDLINE URETERO-URETEROSTOMY NECESSITATED BY A SOLITARY DAMAGED KIDNEY

EDWIN DAVIS AND (by invitation) LEROY WILLIAM LEE

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The frequency with which unilateral obstructive and fistulous lesions of the lower ureter come to the attention of every consulting urologist, as contrasted with the rarity of case reports of uretero-ureterostomy, indicates failure to take advantage of the opportunity for conservation and protection of renal tissue afforded by this useful procedure. With particular reference to postoperative ureterovaginal fistula, it is our purpose to present one additional case report of uretero-ureterostomy and to advocate consideration of this procedure as a better alternative than ureterovesical or ureterosigmoid transplantation, or sacrifice of the kidney. In our case the easy way out (nephrectomy) was not open, since our problem of correcting a vesicovaginal fistula had become complicated by reason of a previous attempt elsewhere w th removal of the wrong kidney. Available material therefore consisted of an obstructed dilated ureter and hydronephrotic kidney on the left side (fig. 1) and a normal ureteral stump on the right. Other methods failing, uretero-ureterostomy therefore came to be a matter of necessity.

This operation was performed January 1, 1945, and the report, together with a summary of the literature, submitted for publication, although appearance of this paper has been delayed indefinitely for reasons irrelevant. At the time there were only 4 cases to be found in the literature, the first by Higgins in 1935. Subsequently a report by Slutsky appeared, describing a successful uretero-ureterostomy performed under somewhat similar circumstances, in that this patient also had had a nephrectomy several years previously. Since there could be no purpose in duplicating Moore's recent excellent review of this subject, reported before this society 1 year ago, including a résumé of early experimental work as well as clinical results, and bringing the total of the reported cases up to 8 (in addition to Slutsky's case), our summary of the literature has been deleted.

CASE REPORT

Mrs. R. S., aged 39, presented herself with the complaint of vaginal urinary drainage, constant over a period of 8 months, since onset 10 days following hysterectomy for uterine bleeding. Nephrectomy (right), performed elsewhere, was followed by cessation of normal urination, but was without influence upon the amount of vaginal drainage.

Physical examination was essentially negative, although the patient's appearance indicated malnutrition and secondary anemia. Temperature and pulse were within normal range. The chest and abdomen showed no abnormalities excepting low midline scar.

The nonprotein nitrogen was reported to be 56 mg./100 cc of blood, the hemoglobin 10 gm./100 cc of blood, red cell count 4 million, and white cell count 9500. The urine was cloudy and infected.

Vesicovaginal fistula was first excluded by vesical instillation of methylene blue. This observation was then confirmed by cystoscopic inspection which gave no findings other than low grade cystitis. Indigo carmine, injected intravenously, did not appear from either ureteral orifice during a 30 minute observation period, although this dye appeared in the vaginal vault after 10 minutes. Attempted ureteral catheterization (fig. 2) demonstrated an impassable obstruction on the left side, 4 cm. above the orifice, and showed the ureter on the right (nephrectomized) side to be patent. Retrograde pyelography was not helpful.

FIG. 1. *A*, intravenous urogram, showing hydronephrosis which involves solitary (left) kidney; also hydroureter. *B*, showing reflux of opaque medium filling right ureteral stump. Left ureteral catheter obstructed at the approximate 4 cm. level.

Intravenous pyelography demonstrated a definite grade of hydronephrosis and hydro-ureter upon the left side (fig. 1).

Diagnosis: Hydronephrosis and hydro-ureter, left; ureterovaginal fistula and ureteral stricture, left; right kidney, absent; right ureter, normal.

Under continuous spinal anesthesia (method of Lemmon) the lowermost left ureter, exposed by tedious retroperitoneal dissection through a paramedian incision, was found to be hopelessly involved in a mass of dense scar tissue, including bladder wall, stricture and fistula, and extending deep into the pelvis toward the great vessels. Immediately above this mass the ureter was found to be thick-walled and dilated almost to the size of one's thumb. Fixation of bladder and shortness of ureter precluded ureterovesical anastomosis, and implantation into

the sigmoid colon was contraindicated by thickness and dilatation of the ureter. Of the two remaining alternatives, cutaneous ureterostomy or anastomosis to the right ureteral stump, the latter was chosen.

The left ureter was first divided above the scar mass and mobilized as high as possible in order to permit translocation across the midline. To expose the normal right ureter it was necessary to employ the transperitoneal route, including packing off the bowel, followed by retroperitoneal dissection through rather an extensive incision in the posterior parietal peritoneum. The bladder was then opened, the right ureter catheterized, and the catheter, 8 F, brought out through a small longitudinal slit in the ureteral wall at the proper level to pre-

FIG. 2. Combined retrograde and intravenous urogram, 6 months postoperatively, showing clearly the T-anastomosis, with wide lumen, overlying sacral promontory; also a distinct lessening in the degree of hydronephrosis.

vent kinking, and passed into the lumen of the left ureter, through its severed end, up to the left renal pelvis. After having obtained end-lateral approximation, without tension, the anastomosis in two layers with 00000 chromic catgut, was a comparatively simple matter, in that the transversely severed end of the dilated ureter adapted itself quite readily to the longitudinal slit in the normal ureter. In fact, such difficulties as the entire operation presented were associated with location and mobilization of the ureters, rather than with the actual anastomosis. The posterior parietal peritoneum was then closed, covering the site of anastomosis, and routine wound closure carried out leaving 3 Penrose drains in the retroperitoneal space, a Pezzer catheter retained in the bladder with a purse-

string suture, and the ureteral catheter extending from urethra to left renal pelvis by way of the bladder and right ureter.

Considering the extent of the surgical procedure, involving direct contact between peritoneum, retroperitoneal space and lumen of the bladder, the patient made a surprisingly uneventful convalescence, with a maximum temperature elevation of 100.2 F on the second postoperative day. By way of medication, she received parenteral fluids for the first 3 postoperative days and sulfadiazine, 4 gm. daily, for 8 days. The suprapubic tube and the ureteral catheter were removed on the tenth and twelfth postoperative days respectively, and the patient dismissed 10 days later with the incision healed and with normal urinary control, by way of the urethra. There was no postoperative vaginal leakage. Nonprotein nitrogen was reported 35 mg./100 cc of blood, upon dismissal, as contrasted with 56 on admission.

Follow-up examination after a 6-month interval showed the patient in excellent physical condition. She reported a gain in weight of 20 pounds, and herself doing the house work incident to the care of 8 children. Pyelo-ureterographic studies made at this time (fig. 3) showed distinct lessening in the degree of the hydronephrosis and a wide lumen at the site of the anastomosis.

COMMENT

It should be noted that the technique of retroperitoneal exposure, mobilization, approximation, and anastomosis of the ureters is by no means so formidable as one might judge; also that continuous spinal anesthesia is a very important factor in success by reason of providing relaxation and excellent exposure as well as permitting the operator to substitute deliberateness for haste.

In this particular operation, had uretero-ureteral anastomosis been anticipated, the technique could have been simplified and the hazard lessened by preoperative catheterization of the right ureter, thus avoiding cystostomy.

CONCLUSIONS

Transmidline uretero-ureterostomy is technically feasible and merits consideration as a better alternative than nephrectomy in cases of ureterovaginal fistula and stricture of the lowermost ureter, not otherwise remediable.

This procedure, moreover, offers a better late prognosis than ureterovesical or ureterosigmoid transplantation, by reason of elimination of the ascending infection hazard.

Medical Arts Bldg., Omaha, Neb.

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DISCUSSION

DR. WILLIAM P. HERBST, JR. (Washington, D. C.): I do not wish particularly to discuss the papers, but I would ask that perhaps Dr. Montague Boyd and the pyeloscopists would get together and figure out some nomenclature which, in so far as the literature is concerned, would differentiate between fluoroscopic observations of the upper urinary tract and direct observation through an instrument.

MR. JOSE (Australia): May I ask Dr. Aberhart what, in his opinion, is the virus infection that is a cause of abacterial pyuria? I had a case a few weeks ago, very similar to the first case that he showed, only perhaps a little bit more so in regard to the upper urinary tract, and our laboratory isolated from this a virus which they said responded rather like the virus of pleuropneumonia. Unfortunately, the condition could not be repeated because the treatment stopped any further virus being isolated from the urine.

DR. KRETSCHMER: What did you use for treatment?

MR. JOSE: He had the usual arsenical preparations over a period of about 3 months. He got quite well. He got well just now, from being a very sick man.

DR. WILLIAM J. BAKER (Chicago, Ill.): Inasmuch as Dr. Davis has opened up the subject of retropubic prostatectomy, I think it behooves me to state that we have been vaccinated in Chicago but the vaccination hasn't "taken." There are five Class A medical schools in Chicago. That leaves a broad field for teaching. Of course, we have to admit, as Dr. Davis has admitted, that there are many ways of doing the same thing and doing it well.

To my certain knowledge, there are only two places in Chicago where the retropubic is being done. I have done a few, less than a hundred, in self-defense, around County Hospital. Dr. Harry Rolnick has done a few at County and he has done a few in private practice at Mount Sinai Hospital. To that extent, the retropubic has been done in Chicago.

In the few which I have done, I have had no immediate trouble. However, in a place like County Hospital, the personnel varies so much that you are bound to see bad results with the good. In the retropubic operation, I have seen 3 men die of hemorrhage, the only ones I have seen die of hemorrhage during my stay in the urological world. I have seen 8 instances of osteitis pubis. I must confess I hope I never have such an entity. I have seen 2 instances of permanent urinary incontinence from this operation. How in the world that could happen, I wouldn't know but it did. And when I make rounds at County Hospital and see these persistent suprapubic infected areas which you can press on the lower half of the abdomen and cause a good stream of purulent material to exude, I think I am still in the position of doing the operation in self-defense only.

I can see no excuse for this procedure when a man can obtain the same results, or even better, with procedures already at hand. It impresses me as being a suprapubic perineal prostatectomy.

I just throw out these remarks as coming from a center where there are five teaching medical schools.

DR. LOUIS ORR, JR. (Orlando, Fla.): I think it is perfectly natural that from the British Empire should come another suprapubic type of operation for the prostate. You must keep in mind that before Mr. Millin's endeavors along the line of opening the capsule of the prostate from above, perineal prostatectomy was little used in his country.

I might say that it is a relatively simple operation. Perineal exposure is exceedingly easy and the operation can be performed as rapidly as the retropubic prostatectomy.

I might also say that overseas, only relatively few people are doing any considerable number of endoscopic resections. Of the ones I had experience with during the war years and on a visit to England a year ago, they were being done rather badly. If one is familiar with all types of prostatic surgery, the Freyer operation, as it is known in England, endoscopic resection, retropubic and perineal, how does one collect cases in numbers of a hundred or more of retropubic prostatectomy unless the operation is performed simply for the purpose of getting together a series of patients?

We are showing a breakdown of 2½ years' experience with prostatic obstruction at the Los Angeles meeting, and we have followed some 476 private patients. In none of those operated upon did the prostate weigh over 25 gm. In 94 per cent, using digital pressure on the prostate through the rectum, we were able, we sincerely believe, to remove more than 90 per cent of all the obstructing tissue by means of a resectoscope.

In our experience of 25 years, we found that people done in 1932, are going along quite well without recurrence of prostatic obstruction and without residual infection. In that same series there are people upon whom we did suprapubic prostatectomies and perineals who have since had recurring adenomas with obstruction; so I think it is not unusual that our friends from over the water should tell us that the retropubic operation is the thing that is being done over there.

We have had a considerable experience with the retropubic operation down my way, and if you will remember, in Boston last year at the meeting, we presented a film to which Mr. Millin took exception. We honestly tried to show a gland of 135 gm. in size being removed. The blood loss was considerable, and I cannot conceive of pulling an apple through a hole that is only 1 or 2 cm. in width. There is bound to be lateral bleeding; there is bound to be some difficulty.

We have had no osteitis, but as Mr. Millin said when I asked him this question: "What are the advantages of retropubic prostatectomy?", "It is a clean, clear-cut operation through the capsule of the prostate, not through the bladder wall."

I asked, "Do your people get out of the hospital any earlier?" and he said, "They do not."

Another series of patients in England operated upon by the Freyer procedure have been getting out of the hospital in 2 weeks, right along with the retropubic people, so I think, again, from a country which has been utilizing only

one type of operation, it is not unusual to find this large series of cases of retropubic prostatectomies.

Dr. C. D. Creevy (Minneapolis, Minn.): I would like to take this opportunity to say a few words about transurethral resection, but I am not going to, except to point out that it is unquestionably the most satisfactory method of visualizing the prostatic capsule, since that was brought up, and that I feel very strongly that for the average benign obstructing prostate, it is the operation of choice.

However, the point that I wanted make has not been mentioned in connection with retropubic prostatectomy. It seems very clear to me, having seen Mr. Millin do a couple and having performed a few myself, that the secret of successful retropubic prostatectomy lies in its speedy performance. Mr. Millin gets through very rapidly. The patient does not have time to lose very much blood. When I try to do it and fiddle around as I like to do, and as I think one should be able to do with the average operation, the blood loss becomes excessive.

We have measured the blood loss in every retropubic that we have done (which total only about 20), and it has ranged from a minimum of 175 to a maximum of 2200 cc, the last coming mainly from wasting time.

Dr. Aberhart (Closing discussion): It has been rather commonly suggested in the literature that the etiological organism of this disease might be a virus. It has also been suggested in the earlier literature that a spirochete might be responsible. We have been unable to demonstrate either a virus or a spirochete in any of our cases and, therefore, I am unable to answer your question as to what the etiological agent may be.

Dr. Leadbetter (Closing discussion): I simply would like to say that if any of you are interested in using an instrument like this, I would be glad to send it to you. It is obvious that you will never need to use it frequently. I would like to have you use it, see how you like it, and make suggestions.

MARKED RENAL HEMATURIA WITH NEGATIVE X-RAY FINDINGS

JOHN A. TAYLOR

Unexplained renal hematuria is the most humbling diagnosis that one is compelled to make. The urologist has carried on a campaign over the years for the early examination of all cases of urinary bleeding. Fortunately, with his diagnostic instruments of precision, he can most often make a definite diagnosis and institute early treatment which may be life-saving for the patient. Unfortunately, there is that smaller group of cases with hematuria which tests his diagnostic acumen. Even after the most careful cystoscopic examinations, he is compelled to confess that the bleeding is ideopathic—which, according to Ewing, can be translated to mean "I don't know." It is heartening that this group of unexplained cases is a small one. Cahill reported only 29 cases in 14,000 urologic cases seen over a 10-year period. The term "essential hematuria" is used to denote unilateral bleeding of undetermined origin. This term has not been used because all of these cases do not fit in this category. The 5 cases reported here were very interesting diagnostic problems. All had renal bleeding and in none of them could the hematuria be explained with the aid of pyelographic studies alone.

In general, these cases of unexplained bleeding can be divided into five groups; namely, those due to: 1) changes in the blood vessels; 2) infections; 3) minute carcinomas; 4) blood dyscrasias; and 5) the nephritides.

The first class includes the varices and angiomas. McKay et al. recently reported 2 cases with an excellent review of the literature. In this review, they found only 18 reported cases of renal varix and 54 cases of angioma. All the cases of renal varix were operated upon, and all but one had minute lesions. The lesions in most of the cases of angioma were large enough to cause a filling defect in the pyelogram.

In the second group, infections, the lesion may be a chronic papillitis, with or without ulceration. There may be minute calcification at the site of the inflammation. In 1914, Braasch was one of the earliest to call attention to chronic papillitis. Payne was one of the first to call attention to this so-called calcifying papillitis. In this inflammatory group, one could also find pyelitis granulosa and early tuberculosis.

The importance of the third group, early carcinomas, has been stressed by Herman in his *Practice of Urology*, and more recently by him in an unpublished paper before the New York Society. This group of cases will grow in importance with the greater use of the Papanicolaou smears. A case of very early carcinoma was recently reported from the New York Hospital, in which a nephrectomy was done on the basis of three positive Papanicolaou stains with no other clinical evidence of malignancy. This stained smear technique offers unlimited possibilities. The correct staining of the smears and the interpretation require a great

deal of proficiency. There is chance for error. When one has Dr. Papanicolaou's laboratory at his disposal, he can place great confidence in the diagnosis. A word of caution should be spoken for fear that needless nephrectomies be done on the advice of less competent laboratories.

In the fourth group, blood dyscrasias, the diagnosis can usually be made with laboratory tests. One of our cases presented a very dangerous reduction in prothrombin activity without definite cause.

In the fifth group, nephritides, one must think more of toxic nephritis because of the increased use of chemical substance, both in industry and in the home. Carbon tetrachloride seems to be a common offender. There have been numerous cases reported of carbon tetrachloride poisoning, and it is interesting to note that the chronic alcoholic is much more susceptible to this form of poisoning than are others. Carbon tetrachloride also has a wide use for cleaning in the home. More recently, it has been used in the form of Carbona in the process of a dry shampoo. The vapor is a heavy one and forms a cloud about the head, where it is easily inhaled. One of the cases who had exposure in this manner is reported here. There were 3 other cases admitted to St. Luke's Hospital with a similar etiology, one of which was fatal, and an autopsy was performed which showed destruction of the renal epithelium.

TREATMENT

Braasch in the afore-mentioned article reported 77 cases in which bleeding was checked in 26 by catheterization and pyelographic study alone, and 18 which were checked with pelvic lavage. Irrigation of the pelvis with 1 per cent silver nitrate is an acccepted procedure and caused prompt cessation of bleeding in 2 of the cases in this report. It is believed by the writer that methylene blue has a tendency to arrest capillary bleeding. This has been evidenced by the number of patients who, with persistent moderate bleeding, have promptly responded to the administration of methylene blue, either by mouth or with instillation of a 2 per cent solution. This effect of methylene blue has been discredited by many, but has produced results too often to be coincidental. This action of methylene blue was thought to be a local reaction. The cystoscopic finding of completely coated bladders following the oral administration of the drug led to this belief. Allen et al. have recently reported the result of their experiments with toluidine blue which proved it to be an antiheparinoid substance. Toluidine blue-dimethyl toluthianine chloride and methylene blue-methyl thianine chloride are both aniline dyes which are molecularly similar. It may be that methylene blue possesses some similar coagulating properties. A nephrectomy should be done in these cases only after one has had repeated positive smears from a competent laboratory or when serious bleeding is uncontrollable. The treatment of the blood dyscrasias and the nephritides is beyond the scope of this paper.

CASE REPORTS

Case 1. H. S., a male, 67 years of age, was seen on October 1, 1946 because of painless hematuria for 1 month. He had been cystoscoped and told he should

have a prostatectomy. He had no other symptoms except the loss of 12 pounds in 1 year, and the loss of some strength. His past history and family history were irrelevant.

Physical examination revealed no abnormal findings; the blood pressure was 130/84.

Cystoscopic examination showed no residual urine and a normal bladder. Blood was seen to be definitely coming from the left kidney. The ureters were catheterized without obstruction, and clear urine was obtained from the right kidney and very bloody urine from the left. The bladder urine, with a gravity

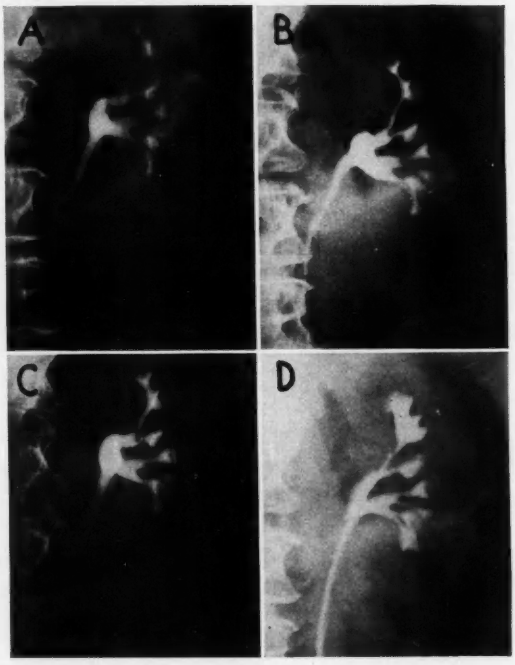

FIG. 1

of 1.023, showed a heavy trace of albumin with no casts, many red blood cells, no pus cells or bacteria. The right kidney urine, with a urea of 1.3 per cent, showed an occasional leukocyte and no casts. The left kidney urine, with a urea of 1.7 per cent, showed innumerable red blood cells and no casts.

X-rays with catheters in situ were negative for calculi. Bilateral ureteropyelograms were done. These showed a tendency towards a congenital type of kidneys, but no apparent deformity in the architecture of the pelvis, except perhaps a slight elongation of the upper calyx of the left kidney (fig. 1, *A*). In order to rule out any new growth, he was advised to have another examination in 4 weeks, and was put on 1 gr. of methylene blue 4 times a day by mouth.

Cystoscopy was repeated on October 31, 1946, with essentially the same findings except that there was less blood from the left kidney (fig. 1, *B*). He reported that his bladder urine had been clear at times during the month.

A third cystoscopic examination was done on January 7, 1947, without any change in the pyelogram (fig. 1, *C*). His blood count at that time showed 12.8 gm. hemoglobin, 88 per cent; 4,440,000 red blood cells; 7,600 white blood cells; polymorphonuclears 74, lymphocytes 24, eosinophils 1, basophils 1. Serology was negative.

Three weeks following that cystoscopy, his urine was clear, and he was advised to stop the methylene blue. He had a recurrence of bleeding, which was quite marked, 2 months later. He was admitted to the hospital, where at this time his red blood cells had diminished to 3,820,000, with 81 per cent or 11.8 gm. of hemoglobin, white blood cells 5,400, polymorphonuclears 62, urea nitrogen 8.1, sugar 75. At this time, his kidney pelvis was irrigated with 1 per cent silver nitrate, following by the instillation of 5 cc of 2 per cent methylene blue. The same day his urine was clear, and he has seen no blood since.

He was seen for follow-up on March 30, 1949. He had no urinary symptoms, felt exceedingly well, and had gained 16 pounds. Cystoscopic examination was done. The right kidney urine showed 2.8 per cent urea, no pus, few red blood cells, and no casts. The left kidney urine showed 2.8 per cent urea, no pus, moderate number of red blood cells, and no casts. A plain x-ray showed no evidence of calculi, and a left pyelogram showed the same architecture as seen on the previous films (fig. 1, *D*).

Comment: This case seems to be one of so-called essential hematuria. The pathology is assumed to have been a minute ulcer about the papillae, which responded to the local treatment.

Case 2. R. M., a man aged 64, was admitted to St. Luke's Hospital on December 4, 1948, with gross hematuria of 24 hours' duration. He had had amoebic dysentery 35 years ago. Repeated attacks of malaria, in China, including one while in a prison camp, but none since his return to the States several years ago.

Six months previously, he had had some precordial pain and had been taking large doses of vitamin E, 75 mg. b.i.d., upon the advice of his doctor.

Physical examination was essentially negative. The blood pressure was 140/90. On admission he had 14.5 gm. hemoglobin, 100 per cent, red blood cells 4,940,000, white blood cells 8,600, polymorphonuclears 74, platelets 200,000, total cholesterol 246, thymol turbidity 1.6 U, urea nitrogen 14.9, and serum protein determinations were normal. Urine showed no growth on culture. Bleding time was 20 seconds, and clotting time 8½ minutes. An electrocardiogram showed posterior coronary pattern.

Cystoscopy revealed no residual urine. There was blood coming from both kidneys, very much more marked on the right, in fact so heavy that there was difficulty in keeping the examining field clear. The ureters were catheterized without obstruction. Phenolsulfonphthalein intravenously appeared in 3½ minutes on the left side in good concentration, and there was a faint trace in 10 minutes on the right, although it was difficult to tell because of the blood. X-ray

with catheters in situ was negative for shadows, and bilateral ureteropyelograms showed what appeared to be a filling defect in the right kidney pelvis and a large kidney on the left (fig. 2, *A*).

The most interesting aspect of his clinical picture was the prothrombin activity. On December 7, 1948, his prothrombin percentage activity was 18. Three days later, the reading showed whole plasma 46, 12 per cent dilute 133, and the percentage activity below 10. At this time, 80 mg. of vitamin K was given, and his prothrombin activity increased to 50 per cent 2 days later, with the subsidence of hematuria. On the fifteenth, his prothrombin activity was reduced again to 27 per cent, and he was given 72 mg. of vitamin K intravenously, with 2 mg. on the next 2 successive days, with a rise in his prothrombin activity to 65.5 per cent.

Retrograde studies done just before discharge from the hospital were quite remarkable (fig. 2, *B*). The filling defect and change in the right kidney pelvis had been due to blood clots with spasm. The pyelogram obtained at this time seemed to show an entirely different kidney than the one at the first examination would suggest. Amoebae were never found in the stools during his stay in the

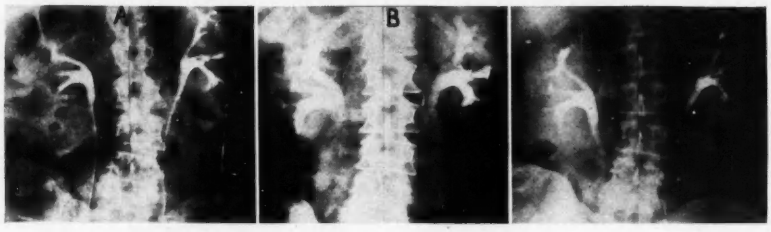

FIG. 2

hospital. He was discharged from the hospital without further bleeding, and had a follow-up cystoscopic examination on January 27, 1949, at which time the bladder urine, with a gravity of 1.015, was negative on chemical, microscopic, and bacterioscopic examinations. The kidney urines were normal except for a few red blood cells from both kidneys, which was probably due to trauma. He states that he has gained weight, that he is taking ferrous sulfate to improve his blood count, and there has been no recurrence of bleeding. The pyelogram (fig. 2, *C*) shows the same architecture as the previous one of December 17. He was seen again on March 8, 1949, when he showed a hemoglobin of 95 per cent, red blood cells 4.50. Urine was negative throughout, and he had no complaints. Two stools had been examined in the interim without finding any amoebae. His prothrombin studies on April 28, 1949 showed whole plasma prothrombin time 17.2, 12½ per cent, plasma prothrombin time 24.0 seconds, percentage activity of whole plasma prothrombin 37 per cent.

Comment: It is believed that these pyelograms are very strongly suggestive of polycystic disease, which are apt to bleed. The fact that he had never bled before would lead one to believe that this hematuria was purely on a basis of the disturbance of his prothrombin activity. This could be explained on the

basis of liver damage due to his dysentery and repeated attacks of malaria over a period of 30 years while in China.

Case 3. N. H., a 52-year-old widow, was admitted to St. Luke's Hospital on December 19, 1948, complaining of gross hematuria of 9 days' duration. She had recently been on an alcoholic bout. She had been painting some furniture a few days before she developed low back pain, and noticed bloody stool plus hematuria. The blood in the stool quickly subsided, but the hematuria continued. She had been in the hospital 5 months before for ulcerative colitis, which was confirmed with x-ray without the finding of amoebae. She had been given the full anti-amoebic treatment, with relief of symptoms.

Physical examination was essentially negative; the blood pressure was 120/60. The liver was slightly enlarged and tender, and the kidneys were palpable but not enlarged or tender. Urinalysis showed 4+ albumin and was loaded with red blood cells. There was no evidence of pus, but a culture did show E. coli. Her blood count showed 4.40 red blood cells, with 85 per cent or 12.6 gm. hemo-

FIG. 3

globin, 10,600 white blood cells, 74 polymorphonuclears, urea nitrogen 8.9, CO_2 55.7.

Intravenous pyelograms done December 21, 1948, were unsatisfactory. Cystoscopic examination the following day showed that the blood was coming from the left ureteral orifice. The left pyelogram seemed to be within normal limits (fig. 3, *A*). The kidney pelvis was irrigated with 1 per cent silver nitrate solution, with prompt subsidence of the bleeding, and she was discharged from the hospital on December 23, 1948.

She had a re-examination on February 3, 1949, at which time the urine, with a specific gravity of 1.008, was negative on chemical, microscopic, and bacterioscopic examinations. The urine from the left kidney showed a urea of 1.1 per cent, and it was microscopically negative. A ureteropyelogram showed the same configuration as the former, except that the pelvis was slightly overdistended with the injection of contrast medium (fig. 3, *B*).

She was re-examined again on April 19, at which time she had no complaints except the aftermath of another recent alcoholic bout. On cystoscopy, the bladder

was normal, and the bladder urine, with a gravity of 1.015, was negative throughout. The right kidney urine, with a urea of 0.1 per cent, was negative on microscopic examination; the left kidney urine, with a urea of 0.8 per cent, showed a moderate number of red blood cells (without red blood cells in the bladder urine, this was considered due to trauma). A left ureteropyelogram was done (fig. 3, *C*) which would seem to rule out any question of renal tumor.

Comment: It is very difficult to explain the hematuria. It may have been due to a small ulceration caused by amoebae. Watters has seen hematuria with amoebiasis. This patient's history, with roentgenographic evidence of ulcerative colitis and improvement on anti-amoebic therapy, suggests that she had amoebiasis in spite of the negative stools.

Case 4. F. R., a 40-year-old male, admitted to St. Luke's Hospital on December 12, 1947, gave a history of developing a chest cold 3 weeks before admission. This was associated with fever, malaise, nose bleeding, nausea and vomiting. Five days before admission, he had gross hematuria with a sharp pain in the left flank. His past history was irrelevant except for chronic alcoholism.

On physical examination, the patient looked acutely ill. The blood pressure was 180/100. He had three clotted bleeding points on his gums. There was bilateral flank tenderness and some suprapubic tenderness. Rectal examination was negative. Urine analysis showed a heavy trace of albumin, and was loaded with red blood cells. Blood count; red blood cells 3.32, hemoglobin 70 per cent or 10.3 gm., white blood cells 10,500. Wassermann was negative. Urea nitrogen was 138.5, sugar 100, creatinine 17.9, platelets 210,000, thymol turbidity 2.0. Bleeding time was 1 minute, clotting time 2 minutes. Prothrombin time 47.5 per cent activity. X-ray examination of the chest was clear.

On cystoscopy, 5 ounces of grossly bloody urine, with clots, were found in the bladder. Blood was being ejected from both ureteral orifices. Bilateral pyelograms were done, which showed what appeared to be a filling defects in both renal pelves caused by clots (fig. 4). Methylene blue solution was instilled in each pelvis.

Further history from the family revealed that the patient had been a heavy drinker for the past 2 years. Three weeks ago, just before the onset of the present illness, he had been cleaning floors with a commercial cleanser which they brought in, and it was found to contain carbon tetrachloride. A diagnosis was made of toxic nephritis due to carbon tetrachloride poisoning. He was treated as a case of lower nephron nephrosis, with a gradual subsidence of symptoms which progressed inversely with the urea nitrogen values. He was discharged on his twenty-fourth hospital day, with a urea nitrogen of 16.6 per cent, and creatinine of 2.8.

At the present time, he is carrying on his normal mode of living, feels well, and refuses cystoscopic examination.

This case was diagnosed mainly with the aid of a good history. It fits the clinical picture of carbon tetrachloride poisoning with bilateral bleeding in a chronic alcoholic.

Case 5. I. B., a woman aged 69, was admitted to St. Luke's Hospital on Octo-

ber 30, 1948. She gave a history of having enjoyed excellent health until 2 days ago, when, following a dry shampoo, she developed gross hematuria with clots in the urine. She complained of no pain in the flank. She had had a cholecystectomy and appendectomy performed 40 years before. She was supposed to have had right ureteral colic 4 years previously, but no stone was obtained.

FIG. 4

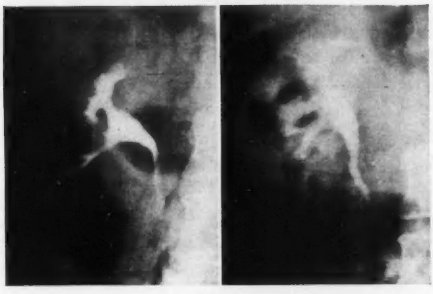

FIG. 5

Physical examination showed a well-preserved woman. The heart was slightly enlarged; systolic murmur was present. Blood pressure 170/90.

Cystoscopic examination showed a normal bladder and blood coming from the right ureteral orifice. The ureters were catheterized easily. The right kidney urine was loaded with red blood cells; the left kidney urine showed many red blood cells. Phenolsulfonphthalein appeared in 3 minutes in good concentration from the left kidney, and none could be observed coming from the right. An

x-ray with catheters in situ was negative for calculi, and bilateral ureteropyelograms showed normal kidneys (fig. 5, *A*) except for the absence of a minor calyx in the right kidney. The blood count showed 4.43 red blood cells, with 85 per cent hemoglobin or 12.5 gm., white blood cells 11,200, p 59 per cent. Urea nitrogen was 16.0, and CO_2 was 44.7. The bleeding subsided following the cystoscopic examination and she has not seen any blood in her urine since. Intravenous urograms (fig. 5, *B*) showed a normal right kidney. It is now 6 months since her bleeding took place. She reports that she has had no further trouble and promises to be re-examined late this month.

Comment: One could not definitely say that this bleeding was due to carbon tetrachloride poisoning. It could easily fit in the picture of essential hematuria. However, with her history, it is probable. The increasing number of cases of hematuria following this form of hair treatment should put the urologist on the alert lest this etiologic factor be overlooked.

SUMMARY

Five cases of renal hematuria are presented: one classified as essential hematuria; another due to a dangerously low prothrombin activity; another possibly due to amoebiasis; and two due to carbon tetrachloride poisoning—one a rather typical case in a chronic alcoholic and the other caused by inhalation of fumes during a "dry shampoo." It is believed that methylene blue is beneficial in the treatment of hematuria.

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RENAL TRAUMA: CONSERVATIVE MANAGEMENT

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Farman, in a carefully documented survey of the literature in this country and on the Continent, on "Traumatic Renal Injuries, Their Diagnosis and Treatment," noted the incidence, which due to the tempo of this modern age, is definitely increasing. He records an average mortality of 20 per cent. He states further that few surgeons have had actual personal experience with more than 10 cases and that the mortality rate in small groups of the most serious injuries is nearer 33 per cent for any plan of treatment.

He describes, first, the pathology or type of lesion as damage to the parenchyma, capsule, pelves and ureters or renal pedicle, and the symptomatology, diagnosis, and finally management.

There is considerable divergence of opinion as to the latter, radical or conservative. At the 1948 meeting of the American Urological Association in Boston, the essayist and members discussing the paper on renal trauma were, in most instances, strongly in favor of prompt surgery rather than conservative treatment, alleging the possibility of delayed secondary hemorrhage, infection, lumbar fistula, cysts with calcification, and hypertension as dangerous sequellae. We are convinced that there are definite and specific indications for prompt and radical surgery in a small number of these injuries, but we cannot subscribe to the view held by many that, owing to the difficulty of establishing the extent of damage or the sequelae mentioned above, the majority of traumatic kidneys should be subjected to immediate exploration after recovery from the state of shock.

We cannot, nor do we wish to, take an arbitrary position on the conservative management of renal trauma; however, in defense of our position and in the hope that it may be of some help in appraising these injuries, we shall submit our experiences with 67 consecutive cases admitted to the surgical service in Mercy Hospital in the past 20 years, 29 of this group admitted to the service of the author in the past 10 years. These cases vary from the mild degree of trauma to the cases with the mutilating injuries, with damage to the viscera and skeletal structures who died of continuous shock a few hours after admission.

AGE AND SEX INCIDENCE

In our group, 58 per cent occurred between the ages of 11 and 30, the period of life when physical activity is at its greatest. For the same reason, renal injury is much more common in men than in women; 59 or 88 per cent in males; 8 or 12.3 per cent in females, which corresponds to the figures from other parts of the country.

CAUSES OF TRAUMATIC KIDNEYS

The incidence has been seasonal. Of the 6 cases admitted to our service in the Fall and Winter of 1947, 4 were football injuries (clipping); 1, sled riding accident; 1, mine injury.

The causes of injuries were fairly equally divided among football, automobile, falls and blows to the back, although in younger children, sled riding accidents were in predominance. It should be remembered that even minor strains may cause renal injury, especially when the kidney is diseased. Herman quotes Bugbee who reported a case of a woman who was dancing with her husband. Coutts believes that congenital anomalies of ribs and vertebra, by causing an increase in the size of the exposed areas of the kidney, are of great importance in the traumatic injuries and found such anomalies in 72 per cent of the cases in his series.

SYMPTOMS

In our group the classical picture of renal injury, the history of trauma, hematuria, gross or microscopic, with varying degrees of pain and tenderness in the flank, was present in all of our cases. Gross hematuria occurred in 62 or 93 per cent; microscopic in 5 or 7 per cent. More than 50 per cent of this entire group were in shock varying from the profound and continuous, which was the cause of death in 3 cases, to the milder forms who recovered when remedial measures were applied. Of the 67 patients, 36 or 54 per cent, were classified as ruptured and 31 or 46 per cent as contusion, in most cases established roentgenologically or by exploration, a few cases diagnosed as such clinically.

DIAGNOSIS

The diagnosis of renal injury is not difficult; the history of injury, shock, hematuria, pain and rigidity in the renal area—a possible loin tumor. The difficulty is in evaluating the extent of the injury and what measures to take to correct it. What criteria have we that will be helpful in a discussion as to conservative or radical management? The extent or character of injury is by no means a guide. Some patients with severe traumatic lesions and clinical and laboratory evidence of renal damage will survive the primary insult, and treated conservatively, will achieve a restoration of adequate or apparently normal function to the damaged kidney. Others with a much less degree of trauma, will have all the evidence of shock and progressive hemorrhage, that will require prompt surgical measures to avoid a casualty.

INTRAVENOUS UROGRAMS AND RETROGRADE PYELOGRAMS

Many urologists advise the use of intravenous urograms and retrograde pyelograms to determine the extent of renal damage and plan their treatment accordingly. In our clinic, intravenous urograms are made on all patients whose blood pressure at renal level is sufficient to excrete the dye.

We have refrained from most of the refinements of diagnosis, feeling that many are unnecessary and may be harmful. It has been our policy to omit cystoscopy and retrograde studies. With Priestley we believe that the history of trauma,

the occurrence of hemorrhage, pain in renal region and the evidence afforded by intravenous urograms in establishing the presence or absence of the other kidney and damage to the injured one, will confirm the diagnosis in most cases.

BLOOD PRESSURE IN RENAL TRAUMA

We have been interested in studying these cases for the possible variations in blood pressure following renal trauma. They fall into three periods:

1) Following the injury, the blood pressure may be lowered from shock; this occurred in 60 per cent of our cases; and in those who did not succumb, the blood pressure was returned to normal, in most cases, as soon as the blood loss was replaced.

2) Shortly following the injury in a number of these cases there was a true renal ischemia followed by rise in blood pressure due to vascular compression from perirenal hematoma, or by packing, in the operative cases, returning to normal after correction.

3) The period in which blood pressure may be altered following renal trauma comes late, after the immediate effects of the injury, when scarring in the perirenal or renal structures may cause ischemia and hypertension. This was observed in only one of the patients in our group.

Numerous writers have suggested renal trauma as an etiological factor in hypertension. Nesbit and Ratliff reported a case of hypertension in which the removal of an injured kidney was followed by temporary lowering of the blood pressure. Braasch and Strom followed 45 cases of renal trauma, treated conservatively, and in only one of those cases was renal trauma considered as a possible factor in the production of hypertension.

TREATMENT

The objectives in treatment are: 1) saving of life of patient, which is the primary consideration; 2) conservation and restoration of function in a damaged kidney. It has been established both experimentally and clinically that the traumatized kidney has a great capacity for repair and restoration of function. In our clinic we have taken the position, in conjunction with most surgeons, that the indication for surgical intervention is necessary if there is evidence of 1) persistent hemorrhage as indicated by falling blood pressure and elevation of the pulse rate or severe anemia, 2) increase in flank tenderness 3) progressive loin tumor, 4) psoas spasm.

All patients with renal trauma, especially of the severer types should have frequent studies in terms of blood pressure readings, recordings of pulse rate and intravenous urograms. If they are not responding to remedial measures, they should be subjected to prompt surgery. Once surgery has been decided upon, it has been our policy to spare as much renal tissue as possible. If incision and drainage of a retroperitoneal hematoma or packing of a hemorrhage is sufficient, we are content with these. Nephrectomy is resorted to only as a last measure when we feel that there is no appreciable amount of renal tissue present that is worth saving or when bleeding from a laceration cannot be controlled by packing.

All 31 contused kidneys were treated medically; i.e., bed rest, fluids, penicillin etc., with no deaths. Three deaths occurred among the group of 35 who suffered ruptured kidneys. All 3 occurred within 24 hours after admission. They could not be aroused from a profound shock enabling surgery to be performed. In 1 case, the lungs were ruptured as well as the kidneys, with hemorrhage into the peritoneal, pleural and pericardial spaces. In another, there was rupture of the diaphragm along with the rupture of the kidney, and severe hemorrhage into the pleural space. Death in the third case was due to cerebral trauma, although the patient had in addition, a fractured pelvis and a ruptured kidney. Of the 32 cases of ruptured kidneys that survived, 2 required nephrectomy on the ninth and twentieth days respectively; 6 required incision and drainage or packing on the eighth, tenth, fourteenth, sixteenth, twenty-third and fourty-seventh days respectively.

No mortality occurred in 64 cases. The overall mortality rate in 67 cases is 4.5 per cent.

We are not unmindful of the later sequelae that may occur in this group, as described by Colston and Baker, and other authors, but we do not believe that in themselves they constitute an indication for immediate or radical surgery. It is our practice to follow up our cases of severe renal trauma by subsequent studies, x-ray and pyelographic, to establish the presence or absence of extra- or intrarenal abnormalities. So far, only 1 case has returned to the department, with any of the complications alleged as indications for prompt surgery. This patient, an 11 year old boy, required nephrectomy 8 months following discharge from the hospital, for persistent hypertension. At operation, a hydronephrotic kidney with marked perirenal fibrosis and vascular compression was removed. The pressure returned to normal after nephrectomy.

CONCLUSION

We have submitted our experience in the management of 67 cases of renal trauma, treated conservatively. As suggested by Kretschmer, we have attempted to crystalize the advantages of conservative management of a large group of these cases; and while recognizing the necessity for prompt and radical surgery in a small group, we believe that if the majority of traumatic renal injuries are submitted to immediate surgery, many of these kidneys will be sacrificed that might have been salvaged if treated in a conservative manner. As a result of our experience with these cases, we feel with Priestley, Power, Sawyer and other surgeons, that conservative measures in the majority of these cases are justifiable.

I am indebted to my residents, Dr. Robert Evert and Dr. Joseph C. Presti for their careful study of these cases and the abstracts of the histories.

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SIMULTANEOUS BILATERAL OPERATIONS ON THE KIDNEYS

THOMAS E. GIBSON

Modern advances in urology have reduced the hazards of renal surgery to a minimum. As a result of more accurate diagnostic methods, improvements in anesthesia, better preoperative preparation and postoperative care aided by the newer chemotherapeutic and antibiotic agents as well as greater knowledge of the physiology of the kidneys themselves in health and disease, operations on the kidneys are today surrounded by safeguards which have reduced surgical risk and mortality to the vanishing point.

Fortunately, very few patients have bilateral surgical lesions of the kidneys. In the small percentage of cases which require operations on both kidneys, it has been the custom in general to operate on one kidney and at some later date to complete the requisite surgery on the opposite side. The literature contains little reference to simultaneous bilateral operations, but the advantages of such a procedure would seem obvious in properly selected cases, particularly in view of the modern safeguards which surround the urological patient today. A limited experience has shown that a good many cases requiring operations on both kidneys can be successfully accomplished at one sitting without imposing undue risk on the patient. It would possess a distinct economic advantage in these days of expensive hospitalization, and at the same time relieve the patient of the dread of having to undergo a second operation at a later date.

In support of this argument one need only call to mind the modern tendency with respect to the radical treatment of cancer of the bladder by cystectomy and ureterosigmoidostomy. A few years ago it was the practice to perform this operation in two or even three stages. Today, as a result of factors already enumerated, it is common practice to carry out the entire procedure in one stage with an even lower mortality than in the multiple stage operation. It has long been common practice in cases of bilateral hernia to operate both sides simultaneously. Although herniotomy is not in the same category as renal surgery in point of gravity, the statistics revealed by Mayo and Hardwick are very enlightening and lend support to our thesis. They found that the incidence of complications and mortality following bilateral simultaneous repair of inguinal hernia is no greater than the combined incidence of complications and mortality following bilateral inguinal herniorrhaphy performed in two operations.

An objection to simultaneous bilateral operations on the kidneys which I think can be over-ruled is that two operations performed at one sitting double the risk and that the longer time needed to accomplish them is apt to result in shock and increased mortality. Now, according to modern surgical concept, time is no longer a factor in morbidity. The important factors are avoidance of trauma, gentle and meticulous handling of tissues, minimizing of blood loss,

and supportive treatment during surgery with clyses and whole blood transfusions, especially when surgical procedures are unduly prolonged. You are all aware of the tedious time consuming operations which neurosurgeons undertake upon the brain, operations requiring 6 to 8 hours or even longer to complete.

In reviewing the literature on simultaneous bilateral renal surgery, only two noteworthy references were found, both dealing with renal and ureteral calculi. The first was that of Hryntschak (1934) of Vienna who reported 15 cases of bilateral stone, 7 of which were operated upon in one stage without a death. He was able to collect from European sources 19 cases in addition to his own, all operated without mortality. The second reference was that of Preistley and Schulte (1942) from the Mayo Clinic. They reported 5 cases of bilateral simultaneous operations on the urinary tract for stone without a death, and advocated this treatment in selected cases. For example, in the event of bilateral ureteral

FIG. 1. Plain roentgenogram, showing small stone blocking right ureteropelvic junction. Tuberculosis of left kidney. Pott's disease. Note calcification in left renal area.

obstruction by stone it would be advantageous to relieve the obstruction on each side at the earliest possible time, especially if a serious degree of infection were present. Furthermore, if a patient had a pyonephrosis on one side and a stone readily removable on the opposite side, bilateral simultaneous operation might be advisable. By this procedure one would not only remove the handicap from the functioning kidney but at the same time by removing the opposite pyonephrotic kidney a potential source of infection and possible postoperative complication would also be eliminated.

Granting the feasibility, and even the relative advantage, of bilateral simultaneous surgery on the kidneys in bilateral calculous disease, the sphere of usefulness of this procedure could be readily extended to encompass other pathological entities. Other conditions, such as a solitary cyst of one kidney and a stone in the other could easily be handled in one stage. In figure 1 is shown a

case presenting a carpet tack type of stone blocking the ureteropelvic junction in an otherwise healthy right kidney, with tuberculosis of the left kidney in a patient with Pott's disease. A right pyelolithotomy and left nephrectomy at one sitting is a rational procedure in such a case.

Hryntschak has enumerated the advantages of the one stage over the two stage operation in dealing with bilateral calculous disease which I have paraphrased as follows:

1) Both kidneys are at once freed of foreign bodies, of infection and stagnation, and as far as possible are restored to normal functional conditions.

2) Local postoperative treatment against infection can be started at once on both sides, whereas if the operation is done in two stages, the infection in the kidney not operated upon persists and is a latent danger to the kidney already treated. Then, too, every operation forcing the patient to become inactive, not only weakens his organism but retards the urinary outflow and this may be

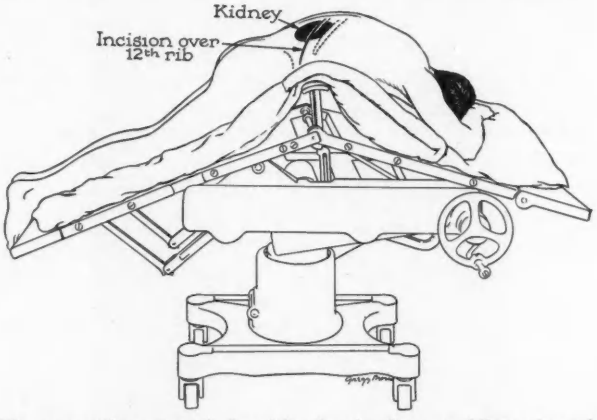

FIG. 2. Diagrammatic portrayal of position for simultaneous bilateral renal surgery

particularly detrimental, as has been demonstrated in those cases in which stone formation takes place after spinal injury.

3) The side not operated upon remains a source of latent danger to the patient, subjecting him to possible complications such as hematuria, colic, blocking of the kidney, fever, pyelonephritis, or even the formation of renal abscesses, all of which are avoided when the complete operation is done in one stage.

4) Every complication which may arise after the first stage may unduly prolong the interval between the two stages to the detriment of the opposite kidney.

5) The patient himself will usually prefer the one stage operation, because once the operation is over he can look forward to final recovery without having to face the prospects of a second operation as serious as the first one, and at the same time enjoy the advantage of a greatly shortened convalescence.

6) The fear that simultaneous bilateral operation might result in anuria is not supported by experience.

TECHNIQUE

The literature contains no reference to surgical approach or technical details in the performance of simultaneous bilateral operations on the kidneys. In the absence of data relative to this phase of the subject we must assume that the

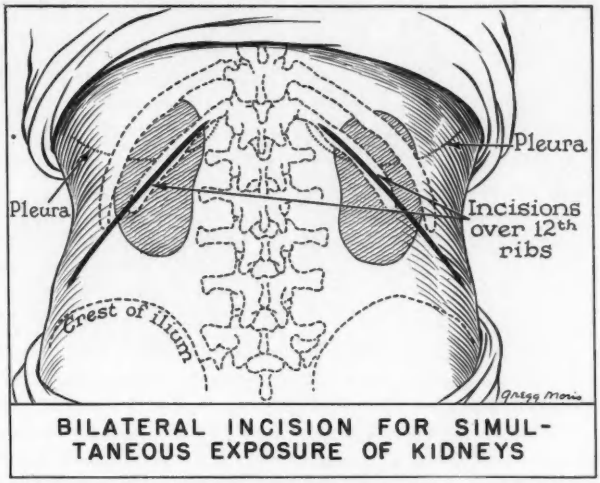

FIG. 3. Sketch showing incisions directly over twelfth ribs which are removed to facilitate exposure of the kidneys.

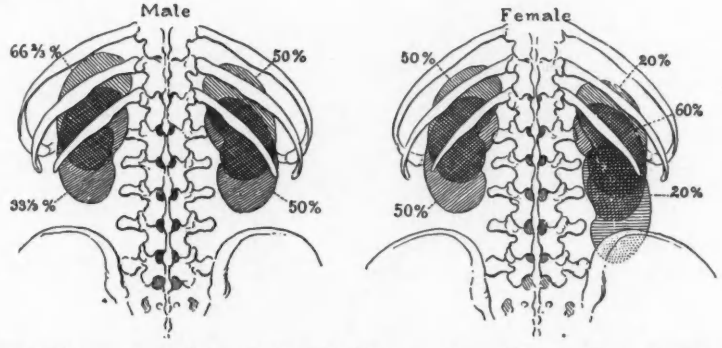

FIG. 4. Diagrams showing positions of kidneys, male and female. The percentages indicate frequency of occurrence. (After Kelly, H. A. and Burnam, C. F.: *Diseases of the Kidneys, Ureters and Bladder*, vol. 1, p. 36, 1954. D. Appleton and Co., New York and London.)

traditional lumbar approach was used, the patient being shifted to the opposite side after completion of the operation on the first kidney.

While operating upon two patients suspected of having adrenal pheochromocytomats by a modification of Young's technique for simultaneous exposure of the adrenals, it occurred to the author that such an approach should be of value

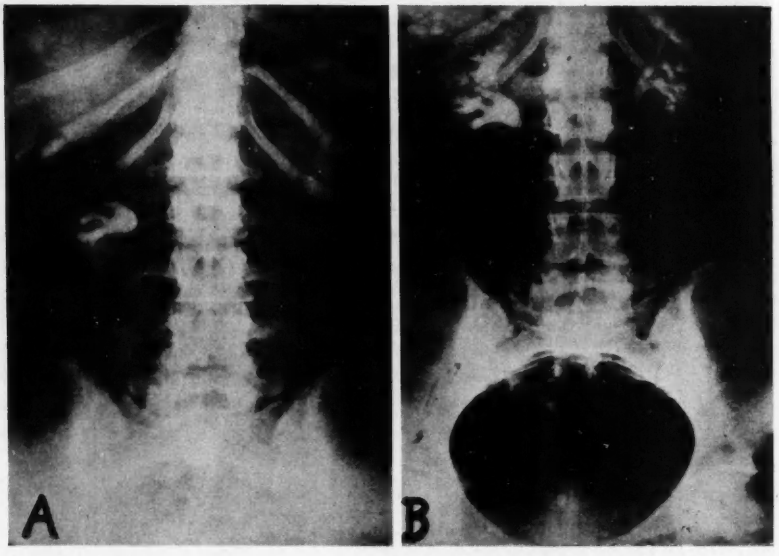

FIG. 5. *A*, plain roentgenogram, and *B*, pyelogram, illustrating staghorn calculus in left kidney of female, aged 40.

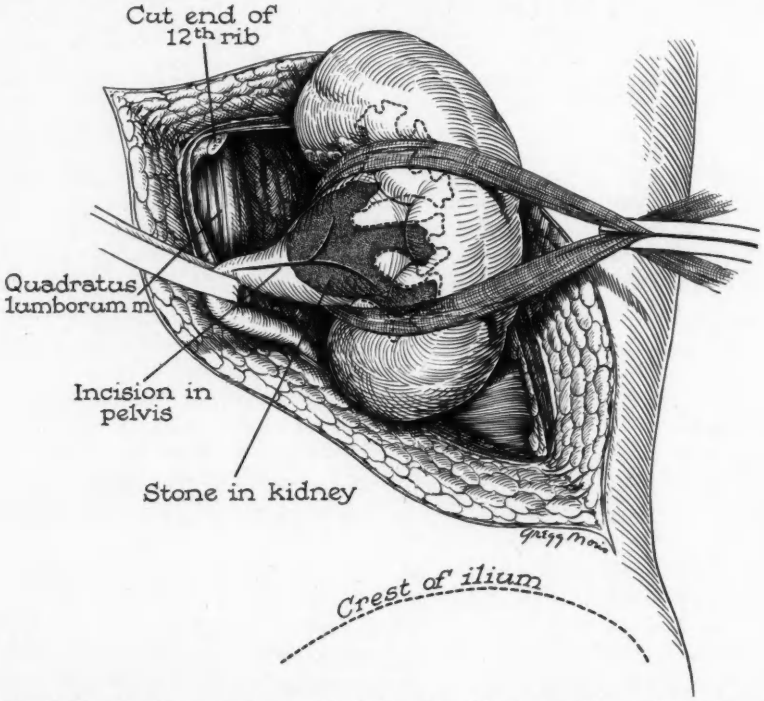

FIG. 6. Drawing from actual operation in dorsal position on staghorn calculus shown in figure 5, showing adequate exposure even though patient was shortwaisted and obese.

in simultaneous bilateral operations on the kidneys. A number of patients have now been operated on by this method and it has been found to give satisfactory exposure, with easy access to the kidneys for any type of procedure one may wish to perform. This approach has the very important advantage that both kidneys may be operated upon simultaneously without the laborious and time consuming task of having to shift the patient from one side to the other and redrape him. Another point to consider is that this position does not demand the extreme lateral flexion of the spine which the conventional position requires, a factor of possible importance in Pott's disease which was present in the case shown in figure 1.

The technical details of the bilateral approach to the kidneys are shown in figures 2 to 4. The patient is placed face down on the operating table, the table broken as desired. In the author's opinion the best exposure is obtained by making the incision directly down on the twelfth rib which is removed. The retroperitoneal space is opened well anteriorly (at the point where the end of the twelfth rib was situated before its removal) and the tissues retracted toward the costovertebral angle so as to minimize the danger of entering the pleural cavity.

In figure 5 is shown the pyelogram of a female patient, aged 40, who was selected as a test case for this surgical approach since she was obese and short-waisted. Figure 6 is a drawing made to illustrate the exposure obtained at operation in this case. Although adequate, this approach is not proposed as one to supersede the conventional lumbar approach in unilateral conditions, since a limited experience seems to indicate that it probably does not afford quite the same freedom of exposure.

CONCLUSIONS

Simultaneous bilateral operations on the kidneys have a definite field of usefulness and well defined advantages in certain cases requiring bilateral renal surgery.

A technique of surgical approach is described which is of particular value in cases suitable for simultaneous bilateral operations on the kidneys.

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GIANT HYDRONEPHROSIS OF TRAUMATIC ORIGIN: A CASE REPORT

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Massive hydronephrosis whether of congenital or traumatic origin is a clinical entity in which errors of diagnosis are frequent due to the silent development of this pathologic state. A large size is attained with a paucity of symptoms due to the absence of infection. However, Wyrens recently reported a huge hydronephrosis due to an obstructing calculus, which sac had evidently been infected for quite sometime. Usually the presence of infection leads to inflammatory changes in the renal parenchyma and pelvis which prevent expansion of the sac; furthermore, pain and toxic symptoms appear which induce the patient to seek medical attention earlier.

Stirling, who originated the term "giant hydronephrosis" as applicable to any kidney containing 1000 cc or more of fluid, reported 26 cases with an error in diagnosis in 7. Howze reported 32 cases with diagnostic errors in 11. Zimet and Kappel contend a wrong diagnosis is made in 1 out of every 3 cases of giant hydronephrosis. Tolson, Wyrens, and Cornwell, each reported a case previously treated for congestive heart failure. The latter author's patient had an abdominal paracentesis performed for ascites thought to be due to heart failure.

A review of the literature gives an erroneous impression of the incidence of giant hydronephrosis, because every experienced urologist has seen at least 1 case of this type. Stirling was able to collect only 74 cases in a review of the literature up to 1939. Hoffman increased this number to 89 in a review up to January 1947. To this he added 10 cases from the records of the Massachusetts General Hospital from 1941 to 1946 inclusive. Wyrens added 1 case in 1949, thus bringing to 100 the total number of reported cases of giant hydronephrosis to this time.

Most authors write that hydronephrotic kidneys which eventually reach giant proportions are usually caused by some form of congenital obstruction at the ureteropelvic junction. Trauma as an etiologic factor has been attested by Meltzer, who, in a review of the literature discovered 18 authenicated cases which occurred months or years after an antecedent history of trauma. He also reported a case which brought the total to 19 cases. The traumatic principle is upheld by Eisendrath who contends that ureteral stricture can develop from trauma to be followed by a late sequela of hydronephrotic change in the injured kidney.

Wagner's classic description of the types of injuries which eventuate in the production of traumatic hydronephrosis are: 1) injury to the ureter, which may coexist with injury to the kidney. Usually the trauma to the ureter is in the upper portion just below the pelvis. The ureteral wall may be crushed or torn and

partial or total stricture develops at the site of the injury. 2) Perirenal or perureteral extravasation of blood, which, through compression may bring about obliteration of the ureteral lumen. With parenchymal injury and rupture of the renal capsule, a large hematoma forms. Only part of this is absorbed, the residual clot becomes organized by newly formed connective tissue. This eventually shrinks and causes distortion or constriction of the ureter.

CASE REPORT

W. W., a white man aged 24 years, was admitted to the gastro-enterological service of Hahnemann Hospital January 5, 1947, complaining of painless swelling of his abdomen and intermittent bouts of hematuria.

His past personal history was very significant, but helped to confuse the diagnosis. In 1937, his right leg had been amputated in the mid-thigh region for a proven osteogenic sarcoma. The convalescence was uncomplicated and he ambulated well with a prosthesis with no complaint referable to his stump.

On October 11, 1942, about 5 years later, while driving an automobile, he was involved in an accident. The steering wheel struck him a forceful blow in the upper left abdomen. He was not rendered unconscious, but experienced severe left upper abdominal and loin pain for which he was immediately hospitalized. Because of severe and persistent pain with marked hematuria, an exploratory operation was performed on the left kidney. A transcript of the operative record indicated the finding of a perirenal hematoma and a contused kidney. Direct confirmation was obtained from the operating surgeons that the kidney was sufficiently visualized at that time to ascertain its normal size, and that no excessive manipulation was required for its thorough inspection. The perirenal space was drained and the wound closed. His postoperative course was uneventful and he was discharged 27 days after the operation.

He was asymptomatic until November 1945, 3 years later, when he first noticed some abdominal distension. This gradually increased over a period of 8 months and he was re-admitted to the same hospital June 1946. At that time he had an added symptom of hematuria of 6 weeks' duration.

Abdominal metastasis from the osteogenic sarcoma of the tibia necessitating amputation in 1937 was suspected. A paracentesis was performed and three liters of dark brown fluid were extracted following which the abdominal enlargement disappeared; also the gross hematuria. A total of 6 paracenteses were performed at intervals of about 1 month.

May 1946, a cystoscopic examination was performed at which time difficulty was experienced in passing a catheter through the left ureter and no urine drainage was obtained. An urogram showed a nonfunctioning left kidney. September 1946, a retrograde pyelogram identified a large hydronephrotic kidney on the left side. The patient was discharged from the hospital with a diagnosis of abdominal metastasis from the previously removed osteogenic sarcoma.

Physical examination, January 1947, at the time of his admission to our hospital, revealed a young, white male, alert and in no acute pain or distress. The abdomen was moderately distended with fluid. No masses or areas of ten-

derness were present. The liver was not enlarged. Neither kidney could be palpated and there was no costovertebral tenderness. The blood pressure was 110/80. The heart and lungs were negative by auscultation and percussion.

Blood studies showed the following: blood urea nitrogen 14 mg. per cent, serum albumin 3.9, serum globulum 2.6, total protein 6.5 mg. per cent, hemoglobin 12.4 gm., red blood cells 4,700,000, white cell count 6,400 and Wassermann negative. Urinalysis on admission revealed 10 to 15 red blood cells per high power field and 40 to 50 pus cells per high power field. Following paracentesis there was an appreciable decrease in the number of white and red cells in the urine. Phenosulfonphthalein test (intramuscular) appeared in 8 minutes; 45 per cent of the dye was eliminated in the first hour and 10 per cent in the second hour.

Two days after hospital admission a paracentesis was performed and 5800 cc of a sero-purulent fluid was obtained. Paracentesis repeated 2 days later yielded

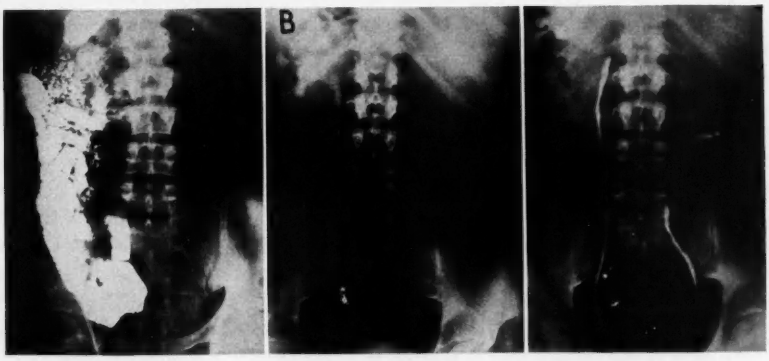

FIG. 1. *A*, complete displacement of transverse and descending colon along with small intestine to right side of abdomen. Upward displacement of stomach. *B*, urogram (15 minutes), showing some calectasis and pyelectasis in right kidney. Right ureter partly outlined. Dye in fundal portion of bladder. Nonfunctioning left kidney. Barium meal remaining in appendix. *B*, retrograde pyelogram. Right renal structures faintly outlined. Marked left ureteral displacement. No renal visualization.

3000 cc of a similar type of fluid. Smears from this fluid showed polymorphonuclear and mononuclear cells. Cultures were sterile.

Following paracentesis no abdominal masses of either kidney could be palpated.

A gastro-intestinal series (fig. 1, *A*) showed complete displacement of the intestines to the right side of the abdominal cavity with upward pressure against the greater curvature of the stomach, which occupied a high and rather transverse position.

Intravenous urography (fig. 1, *B*) revealed relatively normal dye excretion on the right side with a moderate degree of hydronephrosis. On the left side there was no evidence of opaque dye excretion up to 90 minutes after injection.

Roentgen films of the chest were negative for metastatic or other pathologic lesions.

An urologic consultation was requested because of the urographic finding of a nonfunctioning left kidney. Cystoscopy and retrograde pyelography were done

February 1947. Examination of the bladder revealed no gross abnormalities other than a small ureteral orifice on the left side with no evidence of peristalsis. Indigo carmine appeared in good concentration from the right kidney in 4 minutes, none from the left in 20 minutes. The right ureter was catheterized with ease and clear, sterile urine obtained from the right renal pelvis. A No. 6 ureteral catheter passed readily through the left ureter for a distance of 20 cm. where an obstruction was encountered; there was no urine drainage. Analysis of the common urine showed pus 4 plus, red blood cells 2 plus; on culture Proteus morganii was grown.

Retrograde pyelogram (fig. 1, *C*) revealed a mild pyelectasis on the right side without evidence of inflammatory or obstructive phenomena. The left ureter curved medially in the lower lumbar segment, then outward to the left to an abnormal position for the normal ureteropelvic junction. A small quantity of Skiodan solution was injected, but was found to drain down the ureter and would not enter what appeared to be a large hydronephrotic kidney. It was our impression that the mass causing intestinal displacement was extraperitoneal and undoubtedly renal in origin. Transfer for renal surgery was advised.

The gastro-enterological service was not completely convinced and requested peritoneoscopy. The instrument was introduced through a small incision in the right lower abdominal quadrant, 4000 cc of fluid was withdrawn, a culture of which showed Proteus morganii, the same organism grown previously from a specimen of common urine. The peritoneoscopist expressed the opinion that it was like looking into an organless abdominal cavity.

The patient was transferred to the urological service and a left nephrectomy performed March 26, 1947, under spinal anesthesia. The kidney was approached extraperitoneally through a curved left lumbar incision. On opening Gerota's fascia a part of the glistening surface of a huge hydronephrotic sac bulged into the wound. To facilitate removal of the sac its contents were aspirated. The upper pole of the hydronephrotic sac extended to the diaphragm and the lower pole deep into the pelvic brim. The medial aspect extended well beyond the midline of the abdomen. Using sharp and blunt dissection the hydronephrotic sac was removed in toto without great difficulty. At no time during surgery did the patient display any evidence of shock.

The postoperative course was uneventful and the patient was discharged on the twelfth postoperative day. He was followed for a 6 month period during which time there was no recurrent abdominal distension. When finally discharged his wound was firmly healed, the urine was clear and sterile and he was enjoying excellent health.

The pathological specimen was distended in an attempt to simulate its hydronephrotic state. The capacity was 4000 cc and the specimen measured 35 by 17.5 by 15 cm. Inspection of the interior of the sac revealed enormously dilated calyces which were covered with a thin layer of renal parenchyma. Stained sections of the pelvic wall revealed destruction of the epithelial lining with areas of necrosis. Sections of the parenchyma showed tubular degeneration with widely spaced glomeruli separated by fibrous tissue.

The obstruction which had caused the hydronephrosis was found at the ureteropelvic junction. Beginning at the ureteropelvic junction and involving 3 cm. of the ureter below this point was dense cicatricial tissue which included the ureter and peri-ureteral tissue. This caused almost complete occlusion of the ureteral lumen and the ureteropelvic outlet.

DISCUSSION

This case presented several interesting and unique features. The diagnosis was originally confused by a previous occurrence of an osteogenic sarcoma. It was thought that abdominal metastasis not only caused an ascites, but also an ureteral obstruction on the left side to produce a hydronephrosis. The degree of enlargement of the hydronephrotic sac was not realized partly because of the lack of displacement of the ureter which is reported by most authors. The ureteropelvic junction retained approximately its normal position due to fixation in scar tissue which resulted from a perirenal hematoma of traumatic origin.

The presence of hematuria when the patient's abdomen became distended was a puzzling feature. The bleeding must have been the result of necrosis of the pelvic wall about the ureteropelvic junction for no other cause was found on examination of the pathological specimen. The irregularity of bleeding can well be explained by the necessity for a certain degree of positive pressure in the sac in order to have forced the fluid through the stenotic ureteropelvic junction and upper ureter. This would also explain the variations in the amount of pyuria between and after paracentesis.

Although positive cultures were ultimately obtained the contents of the hydronephrosis was primarily sterile, which corresponds to the great majority of reported cases.

Tolson has suggested preliminary nephrostomy to minimize shock from a sudden change of abdominal pressure. Our patient presented no signs of shock either before or during surgery as a result of evacuating the hydronephrotic fluid.

Only 1 case, namely, Cornwell's, was found in a review of the literature, where paracentesis was unwittingly performed directly into the hydronephrotic sac.

In the case presented a total of 9 paracenteses were performed before the origin of the fluid was found to be an hydronephrotic sac. This case is also unique in that it is the first reported where the renal pelvis had been viewed through a peritoneoscope.

The most interesting feature was the ability of the apparently small number of renal parenchymal units to secrete such large quantities of fluid. A known quantity of 3 liters had been removed prior to admission to our hospital; 5800 cc were removed after admission; 3000 cc 48 hours later; and later, 4000 cc at the time of peritoneoscopy. This is strikingly significant of the potential function of renal cortical tissue of hydronephrotic atrophy.

The traumatic origin of the hydronephrosis is unequivocally proven by the presence of a normal kidney found at the time of an exploratory operation for renal trauma in 1942. In less than 5 years a giant hydronephrosis developed which at operation was found to be due to peri-ureteral cicatrization which caused partial occlusion of the uretral lumen.

SUMMARY

An unusual case of giant hydronephrosis with a proven traumatic etiology is reported. It is the twentieth case of traumatic hydronephrosis to be reported, and is the one hundred and first case of giant hydronephrosis to be listed in the literature.

A wrong diagnosis is oftimes made with regard to giant hydronephrosis. In this particular case report the patient was originally diagnosed as having ascites due to metastasis from an old osteogenic sarcoma.

This is the second case to be reported in which paracentesis was performed directly into an hydronephrotic sac.

Medical Arts Bldg., Philadelphia, Pa.

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DISCUSSION

Dr. C. P. Howze (Washington, D. C.): I was very much interested in Dr. Campbell's report, and I thought it might be of some interest to some of you gentlemen to see this film again.

(Film) This is a case that I reported in 1935 before this association. To me, this is really a champion hydronephrosis. This film was taken after draining a liter and a half of clear fluid, after which diodrast was injected and diffused in the sac. As you see, the sac, measuring 11 by 13 inches, fills practically the entire abdomen.

Dr. Edwin Davis (Omaha, Neb.): In commenting on Dr. McCague's paper, I remember an interesting situation which arose some years ago. The case was that of a young man who was badly injured in an automobile accident.

At the time, no operation had been performed and evidently, from the story of long illness and fever, there was an infected hematoma. Later, a nephrectomy was performed, but only after the development of tremendous perirenal fibrosis. This had led, before I saw the patient, to a marked deformity of the body, which was pulled forward; that is, the trunk was pulled forward and toward the side of the injury. He could not straighten up at all. The situation was carefully studied and it was obvious that very extensive surgical operation would be necessary to remove all the scar tissue, and there was no clear assurance that it would not recur.

The patient was an intelligent and determined young man, and he elected not to be operated upon, but knowing the situation, set himself most energetically to a series of exercises, as a result of which, within a period of less than one year, he was able to stand up perfectly straight and was free of all symptoms and was able to return to work. That is just a suggestion as to how such a situation can be handled if the patient is sufficiently determined.

In connection with Dr. Campbell's paper, he spoke particularly of the enormous capacity of the hydronephrosis to excrete a watery urine. It recalled to me a case which is scheduled for publication at a later date—I think it is a rather extraordinary one—in which a patient was admitted to the hospital with a perfectly colossal amount of abdominal distention and also deep in uremia. Eventually, it turned out that he had, on the right side, a hydronephrotic kidney containing 600 cc, and on the left side, a hydronephrotic kidney containing 8500 cc. These kidneys were, of course, treated as quickly as possible by nephrostomy on both sides.

The interesting thing to me is that after the insertion of the nephrostomy tube into the 8½-liter kidney, the drainage at all times, until the kidney was removed, remained purulent and no trace of urine was ever detected in it. Evidently the insertion of the tube had brought about some alteration in the conditions which caused a cessation of the transudation or secretion or whatever you might call it.

Dr. C. E. Burford (St. Louis, Mo.): I wish to make just one plea in regard to renal trauma.

I think we all know, but we probably have not stressed it enough, that in boxing, trauma to the kidney is a serious matter. I have had a number of cases of destroyed kidneys in boxers and wrestlers from kidney punches. One striking case was a man who was formerly welterweight champion of this country, a rather sturdily built fellow. He had in practice, or in training, boxed with his brother who was much heavier, weighing 220 pounds and was on our police force. He had encouraged his brother to punch him over the kidneys to toughen him against kidney attack. He said after each of those training bouts, he had had hematuria. When I saw him, his kidneys were both merely shells, and he died 2 years later, following a slight attack of pneumonia.

Another case was one of our famous wrestlers, known over the country, a university graduate and a most intelligent man. He weighed about 240 pounds. When I saw him, he had but one kidney. The other kidney had been removed on account of an infected hydronephrosis in Los Angeles, where he almost died because the renal pedicle got away from the operator.

Another case worth reporting is that of a man weighing 180 pounds, sitting at his desk when a friend gave him a slap on the back with the open palm and ruptured the pelvis of his kidney. When seen for the first time some days later he was septic and kidney was removed.

I make a plea for barring the kidney punch to conserve the health of athletes. The kidney punch is devastating, crippling and I think we should go on record for barring kidney punches in boxing.

Dr. E. J. McCague (Pittsburgh, Pa.): I should like to ask Dr. Gibson what anesthetic agent he used in operating upon these patients? Is there any contra-indication to spinal?

Dr. James T. Priestley (Rochester, Minn.): The approach which Dr. Gibson has suggested for simultaneous exposure of both kidneys may be helpful in answering a problem which heretofore has not been satisfactorily solved. It perhaps could also be employed for bilateral exploration of the adrenals at the same time.

In my experience simultaneous operation on both kidneys is seldom indicated unless an acute condition, such as obstruction, exists on both sides. In the few cases in which I have performed this procedure, the patient has always had a more severe postoperative reaction than is expected after unilateral renal operation. If performed in a large series of patients it is quite possible that the operative risk would be higher than if each kidney had been operated on separately. It should be kept in mind for the exceptional case, however, where it may prove most helpful in the immediate bilateral restoration of renal function or elimination of an acute and hazardous renal lesion on the one side as by nephrectomy and the correction of a serious and damaging condition on the other side.

Dr. Thomas E. Gibson (Closing discussion): In reply to Dr. McCague's question, I have used spinal anesthesia very rarely in kidney cases, preferring as a rule inhalation anesthesia or sodium pentothal intravenously. Under the new regime of graduate M.D. anesthetists, the anesthesia is left to their discretion, and may consist of a combination of several types.

THE BLADDER IN FRACTURE OF THE BONY PELVIS; THE SIGNIFICANCE OF A "TEAR DROP BLADDER" AS SHOWN BY CYSTOGRAM[1]

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Two recent cases of pelvic fracture, showing in the opaque cystogram a narrow and elongated configuration which we have dubbed "tear-drop bladder," have prompted us to review the literature in an attempt to determine the cause and significance of this striking distortion (figs. 1, *A* and 2, *A*). We have found several reports on fracture of the pelvis or rupture of the bladder, with reproductions of cystograms having a similar deformity;[2,3,12] however, only one author has discussed its etiology and importance at any length.[1] We do not believe that this bladder pattern in the x-ray is a rarity and believe that with frequent early use of the cystogram as a diagnostic procedure in fracture of the pelvis, it will undoubtedly be seen more commonly.

Because of passenger and pedestrian automobile injuries, there seems to be an ever increasing rate of pelvic fractures and associated rupture of the bladder.[3, 4, 5, 6, 7, 8] In 383 deaths from auto accidents, Bacon and LeCount[4] found 42 cases (11 per cent) with fracture of the pelvic bones. Again, automobile accidents accounted for 75 per cent of the ruptured bladders in a 5-year survey at the Los Angeles County Hospital.[7] Before the universal use of the motorcar, the male pelvis was fractured 10 times more frequently than its female counterpart; but in recent years, the incidence is said to be about equal.[9]

The reported occurrence of rupture of the bladder with accompanying fracture of the pelvis varies from 0.7 per cent[4] to 15 per cent.[10] As shown in table 1, a compilation of some of the larger series reported in the literature reveals a grand total of 1,798 cases of fractured pelvis, with 181 of these (approximately 10 per cent) having associated rupture of the bladder.[4,10,11,12,14,15,16,17,18] A similar computation of 259 cases of fracture of the pelvis accompanied by bladder rupture shows 212, or approximately 82 per cent, extraperitoneal in type, and 47, or approximately 18 per cent, intraperitoneal (table 2).[11,12,13,14,17,18,19] Rupture of the posterior urethra, which occurs frequently with fracture of the pelvis, will not be discussed in this paper.

The bladder, when empty, is situated deeply and safely in the pelvis. It lies in a fascial and muscular bed with the pelvic girdle surounding it. The levator ani and obturator internus muscle lie on either side of the bladder; the rectum (and uterus in the female), behind. Anteriorly the bladder is proximate to the pubic bones with the fatty areolar tissue of the space of Retzius intervening. It is firmly anchored in its position by the urachus above, and by the prostate,

[1] Sabadini, L.: The usefulness of immediate posttraumatic urethrocystograms for diagnosis of rupture of the bladder. Press médi., **19:** 231–232, 1948.

[2] Weens, H., Newman, J., and Florence, T.: Trauma of the lower urinary tract. New England J. Med., **234:** 357–364, 1946.

FIG. 1. Case 1. *A*, cystogram obtained during intravenous urography and retrograde injection. Bladder shows "tear-drop" shape which is primarily caused by perivesical blood and urine. *B*, cystogram several weeks after recovery. Bladder now has normal shape.

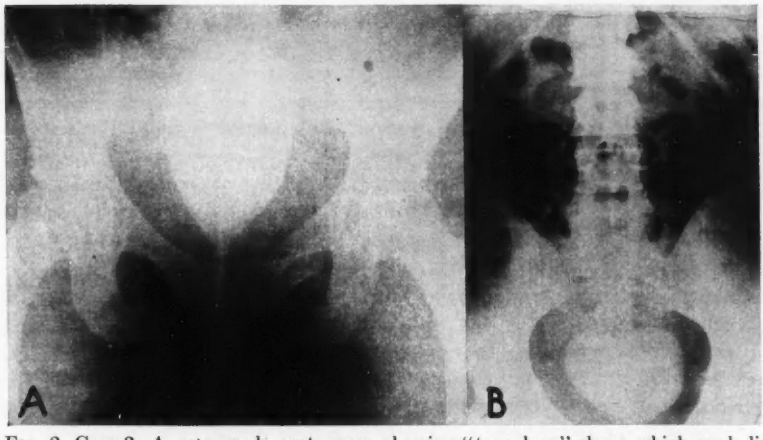

FIG. 2. Case 2. *A*, retrograde cystogram, showing "tear-drop" shape which we believe is caused by extensive perivesical hemorrhage. No evidence of rupture of bladder. No surgery was performed. *B*, intravenous urogram during recovery. Bladder now has a normal shape following absorption of pelvic hematoma.

the medial and lateral pubovesical, and the lateral true ligaments of the bladder below. Laterally and inferiorly is found one of its major anchorages, the "inferior hypogastric wing," which consists of two stout layers of pelvic fascia containing the ureter and the inferior vesical vessels. This structure runs from the inferior lateral aspect of the bladder to the ischial spine.[20] Thus, securely anchored and well-surrounded by substantial structures, it is almost impregnable, when not

[3] Martin, H.: Ruptured bladder. Calif. and West. Med., **36:** 230–232, 1932.
[4] Bacon, L. and LeCount, E.: Automobile injuries. Arch. Surg., **18:** 769–802, 1929.
[5] Peacock, A. and Hain, F.: Injuries of urethra and bladder. J. Urol., **15:** 561–582, 1926.
[6] Stirling, W. and Belt, N.: Traumatic rupture of the bladder with perivesical extravasation. J. A. M. A., **92:** 2006–2009, 1929.

distended, to external injury unless the pelvis is fractured. When empty, the bladder is still vulnerable to external penetrating wounds or to the surgeon's instrument passed transurethrally.

TABLE 1

AUTHORS	YEARS COVERED	NO. OF CASES OF PELVIC FRACTURE	NO. OF CASES WITH ASSOCIATED RUPTURE OF BLADDER
Bacon and LeCount[4]	1911–1924	42	3
Campbell[10]	1919–1928	166	25
McCague and Semans[11]	1905–1942	780	33
Noland and Conwell[12]	1920–1928	125	22
Bogart[14]	1939	51	7
Ashhurst[15]	1895–1908	57	4
Bartels[16]	1878	169	65
Holm[17]	1943	100	3
Gilmour[37]	1920–1929	81	9
Wakeley[8]	1915–1928	100	5
Harding[38]	1929	127	5
Total		1,798	181

TABLE 2

AUTHORS	NO. OF CASES WITH RUPTURE OF THE BLADDER	EXTRAPERITONEAL IN TYPE	INTRAPERITONEAL IN TYPE
McCague and Semans[11]	22*	16	6
Noland and Conwell[12]	22	16	6
Stevens and Delzell[13]	4	3	1
Bogart[14]	7	7	0
Holm[17]	3	2	1
Bacon[18]	72	54	18
Quain[19]	115**	102	13
Gilmour[37]	9	8	1
Wakeley[8]	5	4	1
Total	259	212	47
Per cent		82%	18%

* Eleven of the 33 cases quoted by these authors in table 1 were rupture of the bladder with associated rupture of the urethra and these were not recorded as to extra or intraperitoneal type.

** Twelve cases of original series reported not included. Eight cases were not indicated as to type and four cases were both intra and extraperitoneal.

Rupture of the bladder is not associated with isolated fractures of the sacrum, coccyx, ala of the ilium, ischium or acetabulum.[21] It is directly related to frac-

[7] Crane, J. and Schenck, G.: Rupture of the urinary bladder. Urol. and Cutan. Rev. **36:** 614–619, 1932.
[8] Wakeley, C.: Fractures of the pelvis. Brit. J. Surg., **17:** 22–29, 1929.
[9] Speed, K.: Fractures and Dislocations. Philadelphia: Lea and Febiger, 1935, 3rd ed.
[10] Campbell, M.: Rupture of the bladder. Surg., Gynec. & Obst., **49:** 540–546, 1929.

tures below the pelvic brim, fractures which disrupt the continuity of the pelvic girdle. This type of pelvic fracture is occasioned typically by violent trauma. Lateral crushing injuries such as those which when an individual is caught between two vehicles, result in a double fracture of the anterior pubic portion of the pelvis. There may be a bilateral fracture of both pubic rami or a unilateral fracture of both pubic rami with separation of the symphysis pubis. The detached fragment of bone is small and its displacement is limited by the attachment of many muscles. Trauma in this type of fracture is usually severe because of the relatively prolonged action of the fracturing force.

Anterior-posterior compression, most commonly produced when an individual is run over by the wheel of a vehicle or is involved in a head-on automobile collision, causes a complete disruption of the pelvic girdle. The symphysis is dislocated or the pubic bones fractured; and while the force is still being applied, the posterior portion of the pelvic girdle, at or near the sacro-iliac joint, dislocates or fractures. One half of the pelvis is widely displaced and produces severe trauma.[21,22]

The fate of the bladder in the face of such an injury depends on several factors. Campbell[10] has stated: "The vulnerability of the bladder is in direct ratio to its state of distention." If the bladder is full when the pelvis is fractured, the viscus may be ruptured by direct force in the same manner as it is ruptured without fracture of the pelvis. This type of rupture has been reported in the imbiber of alcohol who falls or receives a blow in the lower abdomen. The rent usually occurs in the posterior-superior surface of the bladder and is intraperitoneal.[25] Tool[23] states that intraperitoneal rupture of the bladder in the female is exceedingly rare. He was able to find only 5 such cases in the recent literature; however, he did add one of his own.

Whether or not the empty bladder is ever ruptured with fracture of the pelvis is questioned by many, although all will agree to the possibility of a perforation by bony spicules.[10] It is granted that the partially or fully distended bladder, inert and heavy, offers ideal resistance to the fractured bone edges and is more easily ruptured by them. Nevertheless, the empty bladder is by no means immune to rupture.[24,25] De Tarnowsky believes that rupture by bony spicules is rare. Apparently this fact is true if one considers the findings of free bony spicules in the bladder as the only evidence that the bladder has been perforated by spicules. It seems entirely reasonable that the fractured pubic bones can be forced into the pelvic tissues and through the bladder wall, or that the vesical wall can be caught between the fractured bones and be perforated. When the fracturing force is relieved, the pelvic girdle resumes its more normal oval outline; the bone withdraws without leaving spicules behind. Another means by which a vesical rent can be produced is a stress on the bladder's moorings (i.e., pubovesical ligaments, inferior hypogastric root, etc.) while the bony pelvis is injured by compression or distortion.

[11] McCague, E. and Semans, J.: The management of traumatic rupture of the urethra and bladder complicating fracture of the pelvis. J. Urol., **52:** 36–41, 1944.

[12] Noland, L. and Conwell, H.: Acute fractures of the pelvis. J. A. M. A., **94:** 174–178 1930.

Perforations of the empty bladder are usually extraperitoneal in type,[25] severe trauma with gross pelvic displacement very rarely causes intraperitoneal rupture.

In brief, it may be stated that with fracture of the pelvic girdle the distended bladder is, by the nature of its incompressible fluid contents alone, more susceptible to rupture. The rupture may be of the "bursting" variety, which is usually intraperitoneal and which accounts for most intraperitoneal ruptures, or it may be extraperitoneal due to perforation by bone edges or stresses on its ligamentous attachments. The empty bladder is much less likely to be ruptured, but it, too, can be torn by bony edges or by strains on its ligament moorings.

Following rupture, urine in the bladder escapes. If the perforation is intraperitoneal, the urine is free to traverse the peritoneal cavity; however, plugging of the rent by bowel or blood clot may temporarily prevent this traversal. The extraperitoneal extravasation usually occurs in the space of Retzius, since most of these lacerations are on the anterior-lateral bladder wall close to the vesical neck.[24,25] From this region the urine may invade the subcutaneous spaces as low as both knees or as high as the umbilicus. Urine can also penetrate the subperitoneal tissues of the pelvis and abdomen and reach the perinephritic tissues.[25] If the urine is infected, it knows no fascial bounds.

In addition to the urinary extravasation, there is the added factor of pelvic extraperitoneal hemorrhage initiated by the pelvic fracture. In close proximity to the anterior portion of the pelvic girdle are a number of vessels which can easily be traumatized when the pelvis is fractured. The pubic branch of the inferior epigastric artery and the pubic branch of the obturator artery anastomose on the posterior surface of the pubis. The deep dorsal vein of the penis goes directly under the symphysis pubis. The internal pudendal vessels and branches, as they course through the urogenital diaphragm, the obturator and superior vesical vessels, and the vesical plexus of veins are all in a vulnerable anatomical position. Additionally, trauma to the muscles attached to the pelvis and injury to the pelvic contents may contribute to the hemorrhage. Meyer[28] reports an extraperitoneal pelvic hematoma following fracture of the pelvis, where the source of bleeding was the internal iliac vein. He was able to see and control the bleeding at operation. In contradistinction, 6 other cases of pelvic hemorrhage from fracture of the pelvis collected and reported by Neller,[27] the source could not be found.

Diagnosis of fracture of the pelvis is usually not too difficult. The patient may be in shock and may complain of lower abdominal pain. Compression of the pelvis may elicit pain. Palpation of the symphysis and of the pubis and ischium by perineal, rectal or vaginal examination will in many cases reveal irregularity of the bones. Neller[27] has emphasized the fact that pelvic retroperitoneal hemorrhage due to fracture of the pelvis gives the same signs and symptoms of peri-

[13] Stevens, A. and Delzell, W.: Traumatic injuries of the bladder. J. Urol., **38:** 475–485, 1937.

[14] Bogart, L.: Rupture of the urinary bladder. Urol. and Cutan. Rev., **43:** 310–313, 1939.

[15] Ashhurst, A. P.: Extraperitoneal rupture of the bladder. Ann. Surg., **49:** 435–440, 1909.

toneal irritation that one sees in intraperitoneal bleeding or ruptured viscus, and that it is almost impossible at times to distinguish clinically among the three.

Culp's[26] statement that "the physical signs alone may be disastrously misleading in rupture of the bladder" is only too true. In intraperitoneal rupture the patient complains of generalized abdominal pain. He is unable to void, or, if he does, a small amount of bloody urine will result. Sooner or later, there is generalized abdominal tenderness and spasm. Free fluid can be elicited in the peritoneal cavity if a sufficient amount of urine has extravasated. Ileus and fever follow soon after. If the urine is infected at the time of rupture, the reaction is quicker and more severe. Extraperitoneal rupture is most often accompanied by lower abdominal pain, tenderness and spasm. The patient may be unable to void or may pass bloody urine, usually with some dysuria.All of these signs and symptoms can be caused, however, by pelvic fracture alone with no bladder rupture.

The signs and symptoms of rupture of the bladder, and for that matter those that indicate fracture of the pelvis, may be insignificant and overlooked if not kept constantly in mind. It should not be forgotten that there may be a combined extra- and intraperitoneal rupture.

The ability or inability to void is of no value as an indication of an intact or ruptured bladder. In 86 cases of fracture of the pelvis below the pelvic brim reported by Campbell[10], 32 or 37 per cent had acute retention and 5 or 5.8 per cent had dysuria, so that about 43 per cent of the cases of fracture of the pelvic girdle, with no demonstrable rupture of the bladder or urethra, had distressing urinary symptoms.

The gross appearance of the urine may be misleading too. The bladder may be ruptured and yet grossly clear urine may be passed (case 1). Conversely, hematuria may occur with no significant injury to the urinary tract. Noland[12] discovered 29 cases of gross hematuria in 125 fractured pelves that had no demonstrable lower tract rupture. Campbell[10] reported gross hematuria in 36 out of 86 cases of fractures of the pelvic girdle with no evidence of rupture of the bladder. Speed[9] states that blood in the urine from microscopic to gross quantities is found in 25 to 35 per cent of all pelvic fractures.

As a diagnostic procedure, the passage of a catheter, with the introduction of a measured amount of fluid and attempt to recover same, is condemned almost universally. In only 13 out of 41 of Campbell's cases was the use of a catheter of diagnostic value. It is a fallacious test with many pitfalls. For example, the bladder rent may be plugged with clot or bowel, and there may be little or no leakage with the introduction of fluid. Then again, the catheter itself may be plugged with clot and thus prevent the extraction of the same amount of fluid that was initially injected. It has been reported many times that the catheter may enter the peritoneal cavity itself via an intraperitoneal bladder laceration and the same amount of fluid injected may be recovered.[10,13]

[16] Quoted by Holm.[18]

[17] Holm, O.: Diagnosis of rupture of the urinary bladder. Acta Radiologica, **24:** 198–205, 1943.

[18] Bacon, S.: Rupture of the urinary bladder. J. Urol., **49:** 432–435, 1943.

Cystoscopy as a diagnostic procedure in rupture of the bladder is not recommended. The additional shock and the possibility of the introduction of infection are two deterring factors. Even more disconcerting is the vigorous and uncontrollable bleeding which renders vision impossible. A large intraperitoneal rent prohibits bladder distention and makes cystoscopic observation impossible.[25,29]

Vaughan and Rudnick's[30] pneumoradiography is apparently fraught with the danger of air embolism. Pelkonen[31] states that 34 out of 791 physicians using this method described cases of air embolism associated with it. Furthermore, in many cases the air cystogram may be very difficult to interpret because of the gas in distended bowel.

The retrograde cystogram, or cysto-urethrogram, is now considered to be the most significant single procedure in the attempt to diagnose a ruptured bladder.[1,2,3,17,18,26,32] It is relatively simple to do a cystogram, when x-rays of the pelvis are being taken, by injecting up to 200 cc of 5 per cent of sodium iodide by way of a catheter. It is likewise easy to inject a portion of the solution through the urethra, thus obtaining a urethrogram, as well. An anterior-posterior view is usually sufficient, but an oblique pcture can be taken without difficulty by lifting one side of the Bradford frame on which these cases are customarily transported.

After the key film has been taken and while preparations are being made to do a cysto-urethrogram, it has been our practice to inject 20 cc of Diodrast intravenously and to take a few films for upper tract studies before and after the cystogram has been taken. Thus, one gets a complete urinary tract study, an invaluable aid in cases of fracture of the pelvis where the injuries are so frequently multiple.

We have found no ill effects from the cystogram. If the opaque medium extravasates, it will be removed or drained at surgery. Careful asepsis should of course be observed throughout the procedure.

The retrograde cystogram is not an infallible method of diagnosis (case 1), but nearly so. The greatest error is probably due to improper interpretation of the x-rays. Culp[26] demonstrated extravasation whenever the retrograde cystogram was used in his cases, and the procedure, in general, is more accurate than the cystogram in the intravenous urogram. But in one of our cases (No. 1) the converse was true. We have been unable to explain adequately the reversal. Cystography by intravenous urography[2,17,33] is attended by certain difficulties. First, there must be adequate renal function. Second, if the bladder is to be completely filled, the intravenous urogram takes much more time than is required by a retrograde cystogram. In addition Holm[17] has suggested that in intravenous urography the medium passes relatively slowly into the bladder and thus may escape through the bladder laceration and be diffused in the tissues, or mixed with the extravasated urine or peritoneal fluid; consequently,

[19] Quain, E.: Rupture of the bladder associated with fracture of the pelvis. Surg., Gynec. & Obst., **23**: 55–62, 1916.

[20] Uhlenhuth, E. et al.: The visceral endopelvic fascia and the hypogastric sheath. Surg., Gynec. & Obst., **26**: 9–28, 1948.

the medium gives only a faint shadow. With the use of retrograde cystography, the medium is instilled rapidly and the x-ray is taken during or immediately after injection. The medium is demonstrated as it passes from the bladder rent.

Weens, et al.[2] have accurately described the appearance of the cystogram in intraperitoneal rupture. Gas distended intestinal loops cast characteristic filling defects in the intraperitoneally extravasated contrast medium. The medium tends to accumulate as a bandlike or linear density along the paracolic reflections. The haustral markings of the colon and loops of small intestine produce a scalloped impression along the inner aspect of the paracolic gutters.

The appearance of the cystogram following extraperitoneal bladder rupture depends on several factors: the size of the rent, the amount of urine in the bladder at the time of rupture, and the extent of the extraperitoneal hemorrhage which usually accompanies the fracture of the pelvic girdle. The most common cystographic appearance of the bladder is that of a vertically elongated narrow bladder, "tear-drop" shaped.[1] The perforation is readily seen with diffusion of the medium from the bladder neck region in a streaked fashion. If the rupture is high and posteriorly located, the configuration may resemble a diverticulum on the posterior superior aspect of the bladder. The medium in this case is blocked by the perivesical edema and the intact peritoneum. If an extensive type of bladder laceration exists, there is a marked diffusion of the contrast material into the pelvic tissues with the medium forming a "sunburst-like" pattern.[1,2]

Fracture of the pelvic girdle without rupture of the bladder, if the accompanying extraperitoneal pelvic hemorrhage is severe enough, can also cause an elongated "tear-drop" shaped cystogram (case 2). Therefore, "tear-drop" configuration is not indicative of rupture of the bladder. One must see the medium outside the bladder in order to make such a diagnosis.

Mortality following a bladder injury depends upon associated injuries, rapidity of diagnosis, and treatment; it also depends upon whether or not the rupture is intraperitoneal or extraperitoneal, or both. The mortality, before 1890, of ruptured bladder from all causes has been given as 86.7 per cent. Following the introduction of aseptic surgery, it dropped to 48 per cent.[19] In recent years it has been quoted as 25 to 36.5 per cent.[11,18] Early diagnosis and treatment are most important; for if proper operative procedures are followed within the first 12 hours after injury, the mortality is 11 per cent. If operation is delayed past 24 hours the mortality is quadrupled.[34]

De Tarnowsky's[25] treatment of urethral drainage and watchful waiting, which he said could be carried out in 5 per cent of cases, is rarely justifiable. We believe that conservative treatment is indicated only in those cases which are extremely poor operative risks because of severe concomitant injuries. Cases have been reported of proven bladder rupture with recovery by means of indwelling catheter alone,[25,35,36] but they are very rare and very fortunate.

[21] Watson-Jones, R.: Fractures and other bone and joint injuries. Baltimore: Williams & Wilkins, 1941, 2nd ed.

[22] Gordon-Taylor, G.: Complicated injuries of the urinary tract. Brit. J. Urol., **12:** 1–28, 1940.

[23] Tool, C.: Intraperitoneal rupture of the urinary bladder. J. Urol., **58:** 431–434, 1947.

Suprapubic cystotomy should be performed as soon as the diagnosis is made and the patient's general condition permits. Provided the rent is intraperitoneal it can readily be found and closed. In intraperitoneal rupture the free fluid is suctioned out and the peritoneal cavity closed without drainage. If there is any question of intraperitoneal rupture, a small incision should be made into the peritoneum and free fluid sought. If rupture is extraperitoneal and is located in the region of the bladder neck, it may be difficult to suture. Cystotomy and extravesical drainage suffice in such cases. Postoperatively, the patient should receive fluids, blood and antibiotics as indicated. When progress of the patient permits, usually 5 to 10 days after suprapubic cystotomy, drainage of urine by uretheral catheter is employed and the suprapubic tube removed.

The following case reports illustrate the problems and progress of 2 patients who showed a "tear-drop" type of bladder by cystography.

CASE REPORTS

Case 1. D.F., an 8 year old white boy, was admitted to the hospital on June 4, 1948. Twelve hours before admission, he was struck by a truck while riding his bicycle. Immediately after injury, he complained of lower abdominal pain and was taken to the hospital, where he was examined by a surgical house officer. Physical examination at that time was essentially negative save for slight suprapubic tenderness. He voided clear urine spontaneously and with no pain or difficulty. He was sent home but about 10 hours later voided grossly bloody urine, returned to the hospital and was admitted to the urological service.

The significant physical findings were limited to the abdomen. There was tenderness and spasm of the lower abdomen with an irregular, tender mass palpable in the hypogastrim and right lower quadrant. No pain was elicited on compression of the pelvis. Genitalia were normal and rectal examination was negative. Urine was grossly bloody.

The patient was immediately transported to the x-ray department on a Bradford frame where intravenous urograms, cystograms, and urethrograms were made. The retrograde cystogram showed elongation of the bladder in "tear-drop" configuration, but there was no extravasation of the medium. Intravenous urograms taken at intervals of 4, 8 and 12 minutes showed excellent renal function; there were no renal abnormalities and the ureters were intact. The bladder, however, showed the same "tear-drop" outline, and in addition there was definite perivesical extravasation of the medium on the right side near the bladder neck (fig, 1, *A*). The urethrogram was normal. Pelvic x-rays showed a greenstick fracture of the ascending ramus of the left pubic bone and some asymmetry of the symphysis pubis.

The patient was taken to the operating room and the bladder was exposed

[24] Cahill, G.: Rupture of the bladder and urethra. Am. J. Surg., **36:** 653–662, 1937.
[25] de Tarnowsky, G.: Rupture of the bladder. J. A. M. A., **95:** 476–482, 1930.
[26] Culp, O.: Treatment of rupture bladder and urethra. J. Urol., **48:** 266–286, 1942.
[27] Neller, K.: Retroperitoneal hemorrhages as a fatal complication to pelvic fracture. Deutsche Ztschr. f. Chir., **227:** 562–567, 1930.
[28] Quoted by Neller.[28]

through a suprapubic incision. There was marked infiltration of the perivesical tissues with blood and urine, especially on the right. The bladder was opened and a linear rent 1 inch in length was found on the anterior bladder wall about one inch above the internal sphincter. The laceration was readily closed with a running 0 chromic stitch. A 26 F de Pezzer tube was inserted into the bladder and the latter closed with running 0 chromic suture. Penrose drains were inserted into the prevesical and right lateral perivesical areas. A 14 F Robinson catheter was inserted per urethram for through and through drainage and irrigation. His postoperative course was uneventful. The sutures were removed on the seventh day; the suprapubic tube was removed on the eighth day. His suprapubic wound was completely healed by the fourteenth day and the urethral catheter was removed. He was discharged on his twenty-fifth hospital day with the advice of the orthopedic service that weight bearing be delayed for two more weeks.

He has been seen regularly in follow-up clinic and has no complaints except a slight limp. Cystogram showed a normal shaped bladder (fig. 1, *B*).

Case 2. C. G., a 19 year old white woman, was admitted to the hospital on April 18, 1948. The patient was riding in a horse show; and while jumping a barrier, the horse struck the obstacle and threw her. Both the barrier and the horse landed on her. While there was no loss of consciousness, she had considerable lower abdominal pain and was unable to walk. Soon after the injury, she voided grossly clear urine with some dysuria.

The following data in the physical examination were recorded: chest, clear; heart, normal; blood pressure, 98/65; and pulse 100, regular. The abdomen was soft, and showed only slight tenderness to deep palpation in both lower quadrants, most marked over the symphysis. The bladder was thought to be percussed three fingers breadth above the symphysis. Rectal examination was negative. Neurological examination was essentially negative.

Additional information was noted as follows: catheterized urine: yellow,acid, specific gravity 1019; negative for albumin and sugar; microscopic examination 10 to 15 red blood cells per high power field, 1 to 2 white blood cells per high power field, hemoglobin, 85 per cent; white blood count, 9,100; stool, guaiac negative.

The patient was placed on constant urinary drainage. Her general condition was good. Portable x-rays confirmed the clinical diagnosis of fracture of the pelvis, and revealed a comminuted fracture of both pubic bones with overriding of the fragments of the superior ramus on the right and with slight widening of the left sacro-iliac joint.

The following day her condition was again good. Her temperature was 100 F; her pulse, 100. There was generalized abdominal tenderness more marked in the lower abdomen, especially on the right. The surgical consultant felt that there

[19] Graham, W.: Management of injuries to the genito-urinary system during war. J. Urol., 57: 73–78, 1947.

[20] Vaughan, R. and Rudnick, D.: New and early sign of ruptured bladder. J. A. M. A., 83: 9–12, 1924.

was no evidence of a ruptured viscus. Urinary output was 900 cc of grossly clear urine which showed 1 to 2 white blood cells on microscopic examination. Hemoglobin was 85 per cent; red blood count, 3,890,000; white blood count, 13,000; and hematocrit, 39.

The second day after admission she was transported to another ward. Soon after this change her general condition became poor; her temperature was 100.5 F; pulse, 120; blood pressure, 100/46. Her abdomen was slightly distended and there was considerable lower abdominal pain, tenderness and slight spasm. Hemoglobin was 48 per cent; red blood count, 2,000,000; and hematocrit, 16. She was given 1,000 cc of whole blood with some improvement in her general condition. The patient was seen by the urological service. A portable cystogram was taken using sterile 5 per cent sodium iodide (fig. 2, *A*). This showed an elongated "tear-drop" configuration of the bladder. The impression of the urological consultant was fracture of the pelvis, bladder contusion and extensive perivesical hematoma.

The third day her condition was about the same. On the fourth day after admission, she remained critically ill. She received another 1,000 cc of whole blood and her blood pressure became stabilized at 128/78. Urine showed 20 to 25 red blood cells per high power field, nonprotein nitrogen 38, hemoglobin 65 per cent, red blood count 3,650,000. She continued to have considerable lower abdominal pain, tenderness and some spasm.

On the fifth hospital day, her general condition was improved. The abdomen was softer with only slight tenderness in the lower quadrants. Temperature was 101 F; pulse, 100; blood pressure, 112/50; hemoglobin, 70 per cent; red blood count, 3,450,000; white blood count, 9,200; hematocrit, 34.

The following day she was considerably improved. Her abdomen was flat and soft and there was active peristalsis. Thereafter, she showed progressive improvement. Her temperature and pulse during the next few days declined to normal. No further transfusions were given, but the blood picture gradually returned to within normal limits. Sixteen days after injury an intravenous urogram showed an essentially negative upper tract and a normal shaped bladder (fig. 2, *B*). On the twenty-sixth hospital day she was transferred to a hospital near her home.

DISCUSSION

These cases illustrate many valuable points in connection with fracture of the pelvis and associated bladder injury.

The difficulty encountered at times in diagnosis is well pointed out by both case histories. In case 1, in which there was a rupture of the bladder, the signs and symptoms when the patient was first seen were minimal. He voided grossly clear urine with no difficulty or dysuria. In case 2, rupture of the bladder was not seriously considered clinically until 2 days after admission when the patient

[11] Quoted by Holm.[12]
[12] Lewis, L.: Cases of severe pelvic injury. Ann. Surg., 121: 470–477, 1945.
[13] Mark, E.: Intravenous urography in diagnosis of rupture of the bladder. J. A. M. A., 100: 42–44, 1933.

had an increase in lower abdominal pain, tenderness and spasm. The lower abdominal signs and symptoms were not due to a ruptured bladder but to a secondary pelvic extraperitoneal hemorrhage, probably initiated by the transportation of the patient from one ward to another. The cystogram proved to be an invaluable aid in this case by ruling out bladder rupture. The drop in hemoglobin from 85 per cent to 48 per cent made the diagnosis of extraperitoneal pelvic hemorrhage almost certain.

Unless the source of the hemorrhage is from a vessel of major caliber, conservative therapy should be practiced when there is pelvic hemorrhage but no rupture of the bladder. Transportation and any other passive movements should be avoided as much as possible in an effort to prevent secondary hemorrhage.

The failure of the retrograde cystogram in case 1 to show the rupture is difficult to explain, as we have said. With the cystogram obtained by intravenous urography, the bladder was filled more slowly, perhaps giving the medium an opportunity to escape through the tear before the viscus attained enough distention to block the rent by resting against the posterior surface of the symphysis.

The cause of the "tear-drop" configuration is primarily perivesical extravasation of blood (case 2), and/or urine (case 1). In addition, there may be an added element of detrusor tetany or spasm occasioned by the trauma.[1] At the time of operation in case 1, there did not appear to be the equal and extensive perivesical extravasation of blood and urine that would seem to be necessary to cause the smooth, even, midline elongation seen on the cystogram; rather, it was confined more or less to the right side. One must presuppose that an added factor, probably detrusor spasm, caused the cystogram pattern seen.

The "tear-drop" bladder is not limited to pelvic fracture with hemorrhage or extraperitoneal bladder rupture or both. It can be present in any pelvic perivesical abscess[2,22] and any extensive pelvic hemorrhage above the levator ani muscles.

That the bladder returns to normal after drainage of the extravasated blood and urine, is illustrated by the normal cystogram taken about 5 weeks postoperatively in case 1. The cystogram in case 2, taken 14 days after the initial retrograde cystogram, shows the rapidity with which the bladder can return to its normal contour following absorption of extraperitoneal pelvic hematoma.

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[1] Negley, J.: Rupture of the bladder. J. Urol., 18: 307–314, 1927.
[2] Culver, H. and Baker, W.: Rupture of the bladder. J. Urol., 43: 511–531, 1940.
[3] Caulk, J.: Rupture of the bladder in a child. J. Urol., 19: 603–611, 1928.
[4] Gilmour, W.: Acute fractures of the pelvis. Ann. Surg., 95: 161–166, 1932.
[5] Harding, M. C.: Fractures of the pelvis. Calif. & West. Med., 31: 320–322, 1929.

THE TREATMENT OF URINARY RETENTION IN WOMEN BY TRANSURETHRAL RESECTION

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Obstruction of the vesical neck in women appears to be of more common occurrence than has been realized heretofore. This is especially true of women past middle life, as attested by the incidence of trabeculation of the bladder encountered in such patients during routine cystoscopy. In the presence of residual urine and definite obstructive symptoms the diagnosis is made easily. Minor degrees of obstruction with little or no residual urine, however, may go unrecognized. Powell has gone so far as to suggest that many female patients with vesical symptoms which heretofore have been attributed to chronic urethritis are in reality suffering from mild obstruction at the vesical neck, even though no residual urine is present. He has been impressed with the results of removing minimal amounts of tissue from the vesical neck by transurethral resection in selected cases.

Obstruction of the vesical neck which has progressed to the stage in which substantial amounts of residual urine or complete retention is present is not so common as the milder varieties; nevertheless, it is not infrequently seen. In spite of adequate articles concerning this subject, these conditions still are diagnosed as "urinary retention of undetermined etiology" or "atypical cord bladder" in too many cases. Also, too many such patients still are allowed to continue with their disability without surgical treatment because of the fear of postoperative urinary incontinence or because the physician is not aware of the fact that in most cases the condition can be treated easily and successfully. Partly responsible for this attitude may be the fact that the majority of articles on this subject have been concerned primarily with the academic problem of the etiology and histopathology of the obstructive process rather than with its treatment. In spite of these excellent articles, there is still much difference of opinion concerning the histopathology of the obstructing vesical neck. Fortunately, exact knowledge of the obstructive process is not necessary to the successful treatment of the condition. Although some comments concerning histopathology will be made, this paper will be devoted primarily to the clinical problem and its cure.

MATERIAL FOR STUDY

A study has been made of the records of all women patients more than 15 years of age on whom transurethral resection of the vesical neck has been performed at the Mayo Clinic during the 9½ year period from May 1938, to January 1948. Patients operated on before May 1938, are not included, as data on them have been reported previously by Thompson. Our search disclosed 100 such patients. On 24 of these patients transurethral resection had been done for neurogenic vesical dysfunction of some type resulting from various types of neurologic disease, such as transverse myelitis, myelodysplasia, tabes dorsalis and multiple sclerosis. Inasmuch as analyses of these cases have been presented elsewhere in articles concerning cord bladder, they will not be included here. This leaves 76 cases for analysis in this study. We have studied the results of treatment in these cases by means of letters of inquiry or periodic examinations of the patient. Adequate data for analysis were secured in all except 13 patients. In these 13 we have used the results at the time of their postoperative dismissal from the clinic.

SYMPTOMS AND FINDINGS

Symptoms complained of by these 76 patients are enumerated in table 1. As one would expect, frequency of urination and dysuria head the list. Many of the patients complained of difficulty in voiding which necessitated straining. Various types of incontinence and urgency of urination were not infrequently seen. Some patients stated that they felt the bladder was not being emptied completely, while more than a third suffered from complete urinary retention or recurring episodes of complete urinary retention. Study of the duration of symptoms (table 2) revealed that approximately a third had been present for 1 year or less, while considerably more than half of them had been present for less than 5 years.

To date it has been a more or less routine procedure for the urologic consultants at the clinic to insist that substantial amounts of residual urine be present before they advise transurethral resections of the vesical necks of women. Because of this, most of the patients in our series carried substantial amounts of residual urine or suffered from recurring episodes of complete retention. Only a very few operations have been done because of marked symptoms of obstruction, in the absence of residual urine (table 3). In view of Powell's recent study, however, it may be found that transurethral resection is indicated for a larger number of selected patients who have symptoms of obstruction without residual urine. Our experience in this regard has not yet been sufficient for us to express an opinion.

The upper part of the urinary tract was studied by excretory or retrograde urography in 52 of our 76 cases. There was evidence of dilatation of the renal pelves or ureters or both in only 13 cases.

We have not been impressed with the constancy of the findings or the value of cystoscopic examination in these cases. Although trabeculation of the bladder

is found commonly, if it is looked for carefully, cases of marked retention are occasionally encountered in which trabeculation is minimal or absent. The cystoscopic appearance of the urethra and vesical neck also may present a conundrum.

TABLE 1. *Frequency of symptoms complained of by 76 patients*

	CASES
Frequency of urination	53
Dysuria, pain and burning on urination	36
Strains to void	29
Nocturia	27
Complete urinary retention, or recurring episodes of complete urinary retention	26
Urgency of urination	19
"Incontinence" (urgency, overflow, stress incontinence)	15
Sensation of incomplete emptying of bladder	13
Hematuria	12

TABLE 2. *Duration of trouble*

DURATION, YR.	CASES
1 year or less	24
2–3	11
4–5	9
6–7	9
8–15	8
More than 15	11
Not noted, or retention discovered accidentally, with no symptoms	4
Total	76

TABLE 3. *Residual urine*

AMOUNT OF RESIDUAL URINE, CC	CASES
None	5
100 or less	11
101–200	15
201–500	10
More than 500	12
Complete or recurring complete retention	22
Not recorded	1
Total	76

At times the cystoscopist can see what appears to be definite obstruction with apparent hyperplasia, hypertonicity or contraction and fixation of the vesical neck from apparent fibrosis or sclerosis. Just as often, however, he sees nothing to account for the obstruction, a normal appearing vesical neck, or even what appears to be an incompetent or relaxed vesical neck and urethra. Also, every

experienced cystoscopist knows that some of the most obstructive appearing vesical necks ever seen are found in patients who have entirely normal vesical function, clear urine and no urinary retention. It is evident, therefore, that decision as to treatment is not made on the basis of cystoscopic findings, but rather on the patient's symptoms and the amount of residual urine present. The urethra and vesical neck should be examined with a fore-oblique telescope or direct vision Braasch cystoscope. A right-angle telescope is not adequate for this examination and a retrograde lens tends to give a false impression of hypertrophy of the vesical neck when it is not present.

TABLE 4. *Age by decade*

AGE, YR.	PATIENTS
16–19	0
20–29	6
30–39	17
40–49	15
50–59	19
60–69	11
70–79	6
80–89	2
Total	76

TABLE 5. *Pregnancies*

PREGNANCIES	CASES
None	20
One	18
More than one	35
Not recorded	3
Total	76

POSSIBLE ETIOLOGIC FACTORS

The cause of urinary retention in the female arouses much interesting speculation. By definition of the cases selected for this analysis we have excluded all cases in which neurogenic vesical dysfunction could be a factor, such as myelodysplasia and spina bifida, inflammatory, traumatic or neoplastic lesions of the spinal cord, tabes dorsalis, diabetic tabes and multiple sclerosis. This phase of the subject has been considered elsewhere.

An analysis of the ages of the patients in this series yields little information (table 4). Apparently the condition may occur at almost any age, although it is most prevalent during middle age. The marital state of the patient should be of interest. Sixty-seven patients were married and 9 were not. This again seems to be of no statistical importance because most women are married.

Pregnancy has been generally considered as a contributory cause, yet table 5 indicates that in this series at least the condition may occur readily in nulliparae.

Surgical operations of various types have been incriminated occasionally. Analysis of our cases showed that previous surgical operations had been done on 16 of the 76 patients. The types of operations were as follows: pelvic surgery in 8 cases; fracture of the pelvis followed by many operations to correct traumatic vesicovaginal fistula in 1 case; removal of the rectum or sigmoid in 3 cases and operations on the bladder or urethra or both in 4 cases. The remaining 60 patients who had not been operated on previously, were studied for possible predisposing factors which might be of importance. The search proved relatively unproductive. Among the few factors of possible importance were the following: old neisserian infection with subsequent stricture and contracture of the vesical neck in 1 case; carcinoma of the uterus or uterine cervix in 3 cases; carcinoma of the urethra and vesical neck in 2 cases; interstitial cystitis in 1 case, and cystocele of marked degree in 1 case. In 1 case the obstruction developed during the patient's fifth pregnancy and was not relieved after delivery. We have been impressed (as have most investigators) with the fact that cystoceles almost never are the cause of urinary retention.

We are left, therefore, with the majority of cases of urinary obstruction and retention in which no contributing cause is apparent. It has been postulated, and possibly rightly so, that long-standing chronic inflammation of the urethra and vesical neck predisposes to fibrosis, contraction and fixation which may prove sufficiently obstructive to result in an imbalance between the detrusor muscle and the vesical neck. This theory certainly seems plausible, inasmuch as the female urethra is subjected to much trauma and infection. As a matter of fact, so-called chronic urethritis is the most common urologic diagnosis made for women. On the other hand, it is difficult to prove from microscopic examination of tissue from the vesical neck that there has been an increase in the amount of fibrous tissue.

HISTOPATHOLOGY

The poorly understood problem of the etiology of obstruction of the vesical neck in women is closely associated with the highly controversial subject of the character of the tissue found at the vesical neck in these cases. The majority of authors who have written on this subject have favored such causative factors as dysectasia, muscular hyperplasia, and inflammatory processes which result in sclerosis, fibrosis, epithelial hyperplasia and edema of the tissue of the vesical neck. Other workers headed by Folsom have championed the theory of hyperplasia or inflammation of urethral glands or of both which they consider to be the homologues of the prostatic glands in the male. To describe this condition they have coined the term "female prostate." MacKenzie and Beck, and Cabot and Shoemaker have presented histologic evidence which they felt contradicted the theory of prostatic glands in women. Guitierrez in a discussion of one of Folsom's papers called attention to the fact that Albarran had described these glands in his textbook. In a previous communication two of us (J. L. E. and J. R. McD.) described the two varieties of glands most frequently encountered in

the vicinity of the vesical neck and proximal urethra. We stated that we had never been impressed with their similarity to prostatic glands. The first variety (subtrigonal or peri-urethral gland of Albarran) is probably the same structure which was described by von Brunn and has been given his name, von Brunn's nests. It would appear to us that if enough sections of these nests were cut, they would not appear to be solid, but rather, lumina would be found. Furthermore, it appears to us that the fluid in these lumina is secretory rather than degenerative in origin. The second variety (the intestinal type of gland) is seen consistently in exstrophic bladders and occasionally in normally placed bladders. It is indistinguishable from colonic epithelium.

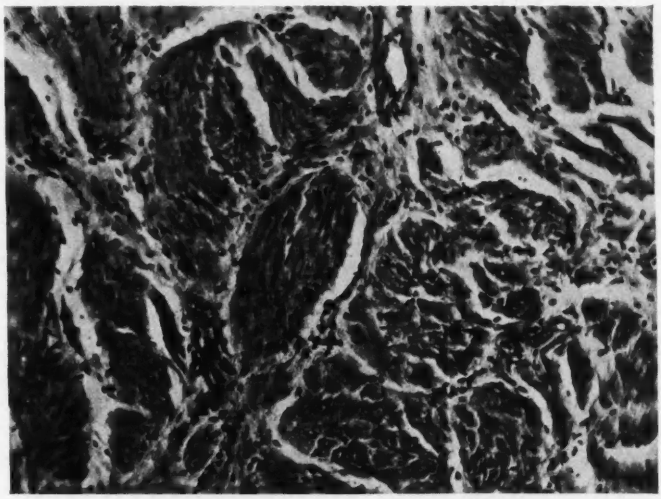

FIG. 1. Normal smooth muscle of vesical neck (hematoxylin and eosin ×125)

In order to obtain as much information as possible regarding the histopathology of the vesical neck, we have studied microscopically the tissue removed from the vesical neck, not only in the 76 cases analyzed, but also in the 24 cord bladders excluded from this analysis. This makes a total of 100 cases studied from a histologic standpoint. The stain used was hematoxylin and eosin.

In practically all of the cases the bulk of the tissue consisted of smooth muscle (fig. 1). In many instances this showed hypertrophy of the smooth muscle bundles (fig. 2). In other words, the muscle cells were enlarged. There was an increase in the volume of the myoplasm and the nucleus. In some instances there was a slight increase in the intermuscular connective tissue whereas normally there is very little connective tissue between the muscular bundles of the normal vesical neck. This fibrosis, however, seemed to be a minor component and certainly does not seem to be a significant factor in the production of obstruction.

Inflammatory cells could be found in practically every instance. These in-

flammatory cells consisted of lymphocytes, plasma cells and polymorphonuclear leukocytes (fig. 3). In addition, newly formed capillaries, namely, granulation

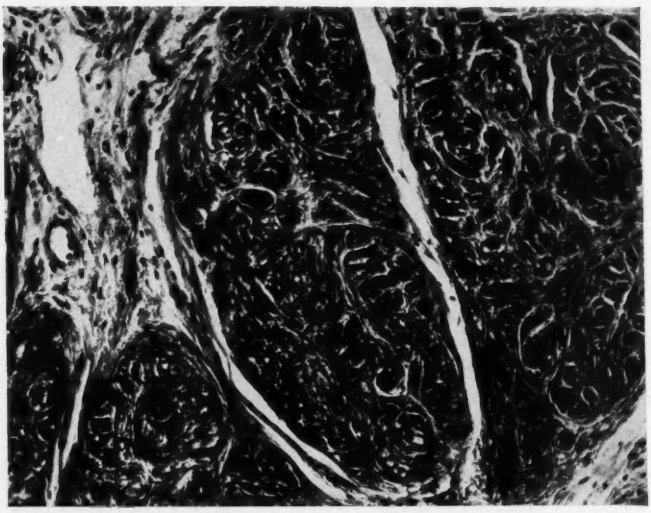

FIG. 2. Hypertrophy of smooth muscle of vesical neck. The muscle cells are enlarged (hematoxylin and eosin ×125).

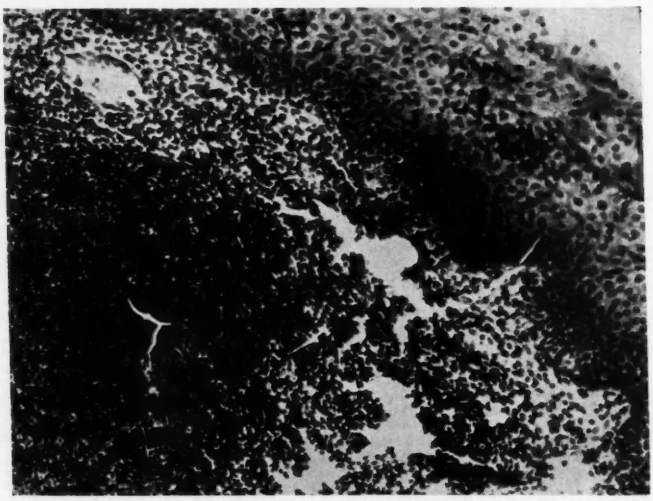

FIG. 3. Subepithelial inflammation. The inflammation is situated beneath the squamous epithelium in the region of the vesical neck (hematoxylin and eosin ×125).

tissue, frequently could be demonstrated. The inflammatory reaction was located between the surface epithelium overlying the vesical neck and the underlying

muscle. It usually was mild in degree. It would seem, therefore, that this played a minor role in the production of obstruction.

The urethral epithelium on the urethral side usually was of the stratified squamous type. On the side toward the bladder, the surface epithelium became transitional. Glands of the subtrigonal type could be found in practically every instance associated with the transitional epithelium (fig. 4). In a few cases these glands or glandlike structures were numerous but in most instances they were few in number. These glands were typically of the subtrigonal type as described by Albarran, consisting of multiple layers of cells with an inner secretory layer of cells having a free border of cytoplasm. The lumen was small and seldom did the glands penetrate to any depth, never into the muscle as prostatic glands

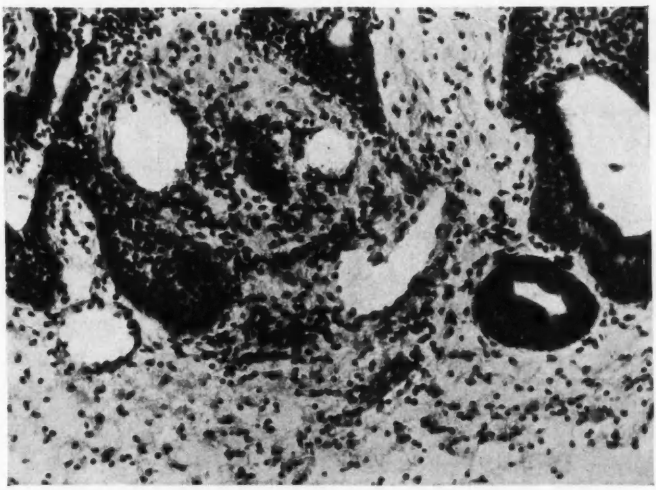

FIG. 4. Periurethral glands of Albarran. The cells lining the lumina are multilayered and the inner border of cells shows a free border of cytoplasm. These glands are situated beneath the mucosa (hematoxylin and eosin ×125).

do. It is possible that these glandlike structures are merely diverticula, rather than true glands but, whatever their nature, the cells lining these structures certainly secrete. Since these glands normally are present in the urethra and in the bladder adjacent to the vesical neck, we could not believe that it is possible to ascribe abnormal qualities to the presence of these glands. It seems unlikely that the obstruction could be the result of the presence of structures such as these. These are the structures which have been described as representing the female prostate, whereas in reality they do not appear to us to represent prostatic tissue. True prostatic glands are, of course, lined by a single layer of epithelium with papillary infoldings and are surrounded by muscle and none of these characteristics pertain to the subtrigonal glands of Albarran.

It would appear from these findings, therefore, that the etiology of obstruction of the vesical neck and urinary retention in the female is not clear. Clinical and

histopathologic findings suggest that numerous factors may be involved, none of which need to be of marked degree to tip the delicate balance of power between the detrusor muscle and the vesical neck.

TREATMENT

Fortunately, from a therapeutic standpoint it is not too important that the etiology and histopathology be known accurately to assure successful treatment. Although only surgical treatment by transurethral resection will be evaluated herein, it should be borne in mind that almost all the patients in the series had previously received the usual conservative types of treatment with unsuccessful results. Transurethral resection was done with the Thompson resectoscope in all cases. In each case tissue was removed from the entire circumference of the neck of the bladder. Experience has shown that the proximal third of the urethra may be safely included in the resection without production of incontinence. The depth to which the resection may be carried without perforation of the bladder depends on the thickness and consistency of the vesical neck. By

TABLE 6. *Number of transurethral resections in each case, and final result of operation*

RESECTIONS		GOOD RESULTS	CONDITION IMPROVED	CONDITION UNIMPROVED
Stages	Total			
1	54	36	12	6
2	15	7	3	5
3	4	2	1	1
4	3	1		2
Total.....	76	46	16	14

experience the surgeon learns how wide the resection may be, but no matter how experienced the surgeon may become, it still is necessary to repeat the operation in a generous percentage of cases. In this series the operation was done in one stage in 54 cases, in two stages in 15 cases, in three stages in 4 cases, and in four stages in 3 cases (table 6). It is surprising how much additional tissue may be easily and safely removed at a second sitting, even though the surgeon feels that the first resection has been done widely. Also, the disturbance of the blood supply at the first procedure leaves the tissue of a consistency which is more easily cut. Care must be taken not to carry the resection too far proximally in order to avoid traumatization of the ureteral orifices. If the patient does not void satisfactorily within a week after operation, the vesical neck should be re-examined and further resection done if feasible. The amount of tissue that must be removed varies tremendously from patient to patient. In some cases only a few small pieces weighing less than a gram are sufficient to establish normal vesical function, whereas in other cases several grams must be removed. The largest total amount removed from any patient in this series was 9 gm.

The results of treatment of these patients have been encouraging (table 6). Good results were obtained in 46 cases; the condition was considered improved

in 16 other cases and was unimproved in 14. The cases in which we have classified the condition as improved can be divided into two groups: 1) those in which minimal symptoms and a small amount of residual urine may have persisted after operation, and 2) those in which an excellent immediate result was achieved but, later on, after several months or years, urinary symptoms or some residual urine or both recurred. It is difficult to evaluate such minimal symptoms from follow-up letters, however, because urinary symptoms in women generally are common. It is our opinion that in many of the cases in which we listed the condition as "improved" a "good result" would have been a more accurate classification. One patient of this type is of particular interest.

A woman, 40 years of age, had some dysuria, residual urine and recurring episodes of complete retention during the second month of her fifth and last pregnancy. This had not corrected itself after delivery. She had become addicted to the use of narcotics and was wearing an inlying urethral catheter on arrival at the clinic. Transurethral resection relieved the retention but the pain continued. Presacral neurectomy relieved the pain, and the patient was dismissed in good condition and with almost normal vesical function. In replying to a follow-up letter more than a year later, however, she stated that she is again being treated for symptoms of pain and dysuria. The extent of her present trouble cannot be accurately evaluated from correspondence.

An analysis of the 14 cases in which poor results were obtained should be helpful in evaluating the general problem involved and the difficulties encountered in therapy. Three of the 14 patients were relieved of their urinary retention but were left with urinary incontinence. In 2 of these cases the retention of urine was caused by an extensive obstructing carcinoma of the urethra, and the operation was done as a palliative procedure only.

In the third case, the patient was a woman 65 years of age. Resection was done because of 300 cc of residual urine. The resection was done in one stage and 3 gm. of tissue was removed. Retention was relieved but moderate incontinence ensued. One year later a Kelly type of plastic operation on the urethra was performed, which eliminated 90 per cent of the incontinence. Since this operation the patient has emptied the bladder completely but has continued to lose just enough urine so that a pad must be worn for protection. It must be assumed that in this case the resection was carried a little too far distally in the urethra.

One patient was a woman 72 years of age, who had urinary incontinence following a posterior resection of the rectum for carcinoma. In addition to the incontinence, examination occasionally revealed 2 to 3 ounces (60 to 90 cc) of residual urine. It was felt that transurethral resection in this case had little chance of helping the patient, but it was tried. Little improvement was obtained by the operation.

In 4 patients the urinary retention persisted after only one resection of the vesical neck had been done. Sufficient experience has now accumulated to demonstrate that resection must be repeated a second or even a third time in a generous number of such patients to achieve a satisfactory result. It seems logical to

assume, therefore, that some of these patients might have been helped by further transurethral resection.

Urinary retention in 5 other patients persisted in spite of multiple resections of the vesical neck. In one of these patients the condition was the result of extensive scarring and fixation of the vesical neck and urethra which had resulted from much pelvic surgery, followed by postoperative inflammation, adhesions, and so forth. It was impossible to eliminate this fixation by transurethral resection. There is no adequate explanation for the failure in the other 4 cases, unless it is assumed that resection was not adequate, even after multiple attempts had been made.

A case in point concerns a woman 48 years of age, who had undergone four transurethral resections of the vesical neck in 4 months, in an effort to eliminate a residual urine of 200 cc. In spite of this, 100 to 150 cc of residual urine continued, although the urine could be kept microscopically clear with an occasional week of treatment with sulfathiazole. A total of 8 gm. of tissue has been removed with the four operations and the urethra is now only half its original length. Another resection will be done later, in the hope that the residual urine may be eliminated.

The remaining case is of interest in that the patient was relieved of her urinary retention for a year or more following transurethral resection done in two stages. Following its recurrence, however, two subsequent resections failed to eliminate the residual urine.

SUMMARY

Obstruction of the vesical neck and urinary retention occurring in women is of more common occurrence than is generally appreciated. There seems to be no one predominant causative factor although numerous predisposing factors may be recognized. Histopathologic examination of the tissue removed from the vesical neck of women in 100 consecutive cases suggests that glandular hyperplasia is not an important factor. It also suggests that most of the glands seen in such conditions are the subtrigonal glands of Albarran, which should not be confused with prostatic glands. Fortunately, successful treatment may be carried out without an accurate knowledge of the etiologic factor involved. Transurethral resection of the neck of the bladder is the treatment of choice.

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THE CONSEQUENCES OF THE SURGICAL RELIEF OF URETEROVESICAL OBSTRUCTION

LOUIS M. ORR

In considering the various factors underlying the cause of hydronephrosis, a study of the literature reveals that very little attention has been given to obstruction at the ureterovesical junction.

Obstructive lesions at this level of the urinary tract are productive of some degree of dilatation of the ureter and renal pelvis above. If obstruction at this point is not relieved, varying degrees of destruction of renal tissue as the result of back pressure will follow. In instances of bilateral ureterovesical obstruction, be it congenital or acquired, the survival of the individual is solely dependent upon some type of corrective procedure designed to relieve back pressure against the renal tissue. The problem of unilateral obstruction of the vesical end of the ureter is not viewed with the same degree of seriousness as effects the survival of the patient, but corrective measures are nevertheless quite important in the general plan of conservation of renal tissue.

To effect satisfactory drainage of the dilated ureter above the point of ureterovesical obstruction requires that the ureteral opening must be enlarged to a caliber sufficient to allow complete emptying of the upper urinary tract into the bladder. It has been demonstrated that in order to properly insure adequate ureteral drainage, the ureteral orifice must be enlarged to such a size that a loss of its valve-like action will follow with an associated regurgitation of the vesical contents up the ureter.

While the production of vesical-renal reflux by surgical means produces an unphysiological state, it has long been known that the existence of reflux of varying degrees is sometimes encountered in normal beings and is no longer considered as being incompatible with good health.

Ritter and Kramer in 1944 discussed the various methods of overcoming ureterovesical obstruction and recited several attempts at resection of the constricted end of the ureter with re-implantation of the severed ureter into the bladder. All of the cases which they reported, with one exception, underwent subsequent nephro-ureterectomy because of failure of the re-implanted ureters to adequately drain the upper urinary tract. The single exception in their series necessitated continued dilatation of the terminal ureter to insure its patency and some doubt was expressed as to the eventual outcome.

Another procedure considered by these authors was lateral anastomosis of the dilated ureter to the bladder wall, but no clinical application of the operation was reported. As a result of these failures at re-implantation of the ureter, Ritter concluded that the procedure most likely to succeed would be one which would enlarge the ureteral orifice to a satisfactory degree and which would not

interfere with the continuity of the ureter into the bladder and would preserve as much peristalsis as possible.

His procedure consisted of first placing a suture deeply on either side of the upper angle of the ureteral orifice and then incising the orifice widely, the sutures purported to aid in preventing undue bleeding and at the same time preserving the size of the opening. Ritter stated that this division of the intramural portion of the ureter left a large gaping ureteral orifice. He did not state whether any type of catheter was left in the ureter to insure patency of the enlarged orifice during healing, nor did he give any long range follow-up report as to whether the enlarged orifice remained a sufficient size to allow adequate emptying of the ureter.

The diagnosis of true obstruction of the lower end of the ureter depends not solely upon finding a dilatation of the ureter in the urogram, but upon the associated presence of retained urine within the ureter. A method to obtain a fairly accurate estimate of ureteral residuum in the presence of possible reflux of uncertain degree is to catheterize the ureters immediately after the patient has completely emptied the bladder, using a measured amount of medium for the cystoscopy. The ureteral contents can then be accurately measured. Even with these two requirements for the diagnosis being satisfied, a cystogram with opaque material under moderate pressure should be made to further ascertain whether any reflux of the vesical contents up the ureter takes place. The degree or absence of regurgitation or reflux will be the determinant in establishing the relativity of obstruction, which is of great importance in making a decision whether or not to enlarge the ureteral orifice.

E. W. Campbell, in an excellent study of the subject of megalo-ureter and congenital hydro-ureter, named as one of the distinguishing features of megalo-ureter the relative patulousness of the ureteric orifice as contrasted to the presence of a normal or narrowed intramural ureteral segment, which is present in congenital hydro-ureter.

During 1946 there came under our observation 2 patients: one a boy of 14 years and the other a woman of 47 years, both of whom presented problems relating to upper urinary tract dilatation due to obstruction at the ureterovesical junction.

The boy was discovered to have enormous dilatation of both ureters with marked tortuosity and moderate hydronephrosis of both kidneys, probably of congenital origin. There was relative obstruction at the ureterovesical juncture with bilateral ureteral retention ranging from 60 to more than 100 cc. There was also marked dilatation of the bladder with gross trabeculation of the musculature of an extreme degree. A residual of 100 to 200 cc of bladder urine was found but no evidence of obstruction at the vesical neck or within the posterior urethra.

The adult was found to have a moderate dilatation of the right ureter with an ureteral retention of more than 30 cc and relative obstruction at the ureterovesical junction, the origin of which was in doubt. The left ureter was found to be slightly dilated and contained only 10 cc of residual urine. The bladder walls revealed no trabeculations and the bladder capacity was normal.

Both patients were operated upon with the purpose in mind of widely opening the lower end of the ureters, thus producing a situation which would allow not only for complete emptying of the upper urinary tract, but for regurgitation of the vesical contents up the ureters, which was presumed to be expected following such a procedure. Both ureteral orifices in the boy were surgically treated simultaneously and the right orifice in the adult was enlarged by the same type of surgical procedure.

OPERATIVE PROCEDURE

Before opening the bladder the juxtavesical end of the ureter is satisfactorily exposed. The bladder is then opened and a grooved director introduced into the

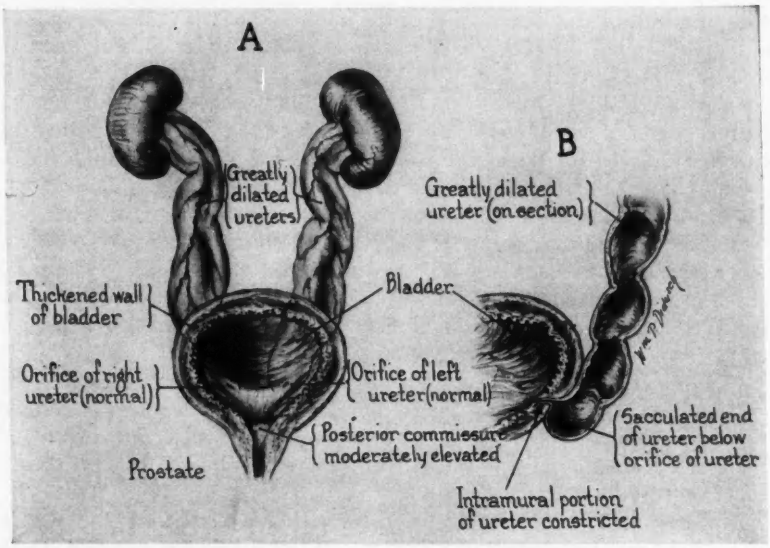

FIG. 1. Diagrammatic sketch showing *A*, markedly dilated ureters and thickened bladder mucosa. *B*, cross section showing sacculation of the lower end of the ureter.

ureteral orifice to serve as a guide. The incision was made in an upward direction through the bladder mucosa and musculature and into the ureter proper. Whenever there is sacculation of the terminal ureter downward behind the trigone, the incision is then carried downward to the bottom of the sacculation, through the trigone. The mucosa of the ureter and the mucosa of the bladder were then united as nearly as possible on either side of the incision with interrupted sutures of chromic catgut (figs. 1 and 2).

This maneuver resulted in a greatly enlarged ureteral orifice being produced. As a final measure a 26 F urethral catheter was introduced through the ureteral orifice and left in place as a splinting catheter to guarantee a satisfactory opening after healing had taken place (fig. 3). These catheters are usually left in for a period of 3 weeks and are withdrawn at the same time, or subsequent to, the

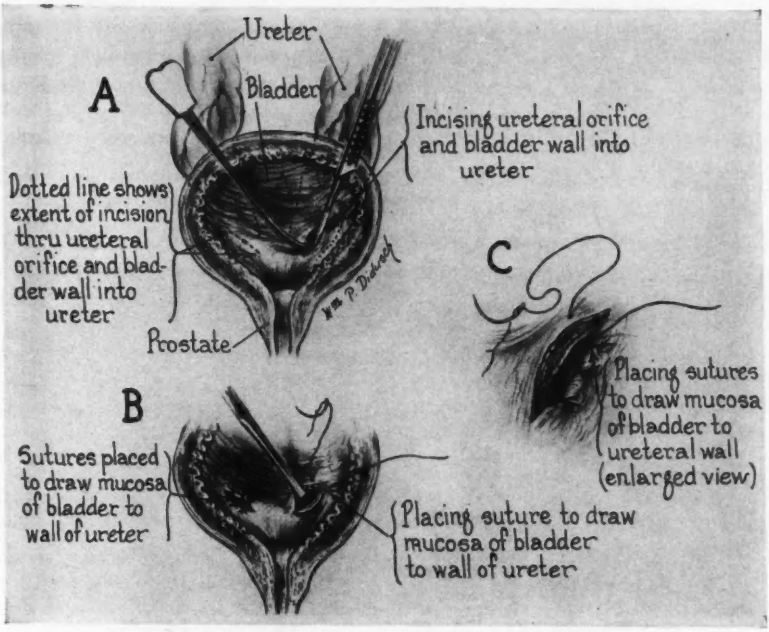
Ureter
A
Bladder
Incising ureteral orifice and bladder wall into ureter
Dotted line shows extent of incision thru ureteral orifice and bladder wall into ureter
Prostate
C
Placing sutures to draw mucosa of bladder to ureteral wall (enlarged view)
B
Sutures placed to draw mucosa of bladder to wall of ureter
Placing suture to draw mucosa of bladder to wall of ureter

FIG. 2. Sketches of surgical treatment of lower ends of ureters.

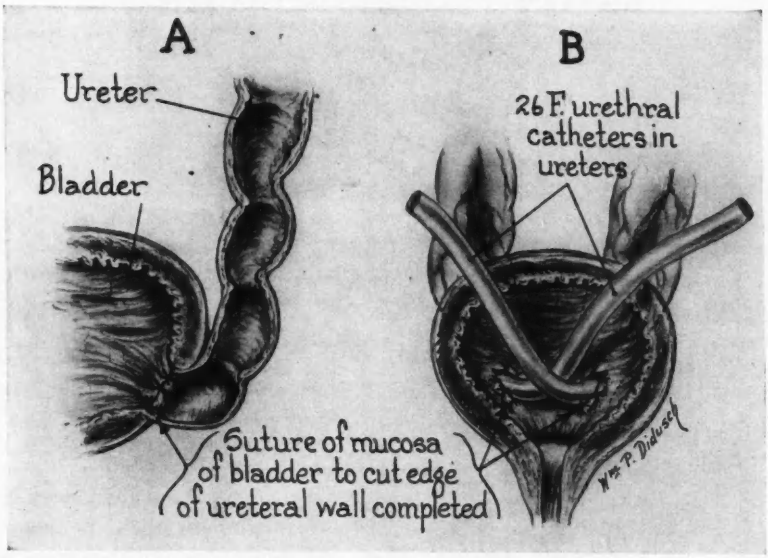

FIG. 3. *A*, sketch showing cross section view of suturing of enlarged ureteral orifice. *B*, Foley urethral catheter in place to guarantee patency of newly constructed ureteral orifices.

removal of the suprapubic tube. In the three ureters upon which this procedure has been carried out, the resulting ureteral orifices have maintained their patency and after 2½ years have functioned most adequately. While this procedure is similar to that of Ritter and Kramer in principle, provision is made for greater permanency of result by the placement of indwelling ureteral catheters and more precise suturing of the enlarged orifice.

CASE REPORTS

Case 1. Mrs. W. V., a 47 year old white woman, was first seen October 31, 1946, complaining of bouts of recurrent pain in the right flank for the past 14 years. When the pain was first noted the patient was subjected to an appendicectomy without relief of symptoms. At varying times the pain had been associated with chills and fever, frequency and burning on urination. Various cystoscopic examinations had been carried out in the years past and long periods of dilatation of the right ureteral orifice had been practiced without success. Incision of the ureteral orifice with cystoscopic scissors and other instruments had been recommended but had never been carried out.

Physical examination revealed a well developed and well nourished adult weighing 64 kg., who presented no unusual findings with the exception of tenderness to percussion and palpation over the right costovertebral angle. Neither kidney was palpable. Examination of the catheterized urine showed no unusual elements. Blood studies were all within the limits of normal.

A cystoscopic examination revealed a normal bladder wall. Ureteral catheterization, using No. 6 catheters, revealed a pelvic retention on the right of 30 cc and on the left of 10 cc. Phenolsulfonphthalein injected intravenously appeared from the right catheter in 4 minutes and from the left kidney in 2½ minutes. The value in 15 minutes from the right was 12½ per cent and from the left 27 per cent. Retrograde pyelograms in the prone position revealed hydronephrosis and hydro-ureter on the right with almost complete retention of the dye in the right kidney and ureter after 30 minutes in the upright position (fig. 4, *A*). The right ureter measured 3 cm. at its widest point.

The patient was operated upon on November 15, 1946, at which time a plastic procedure, as has been described, was performed on the lower end of the right ureter. The postoperative course was entirely uneventful with no temperature elevation above 101 F, which occurred on the second postoperative day. Eighteen days postoperatively the right ureteral catheter was removed and on the twentieth postoperative day the suprapubic tube was removed and a Foley catheter introduced through the urethra into the bladder. Twenty-six days after the operation the Foley catheter was removed and the patient was discharged home 27 days after operation with the suprapubic wound completely healed.

Since the operation the patient has been entirely comfortable with no recurrence of pain in the right flank with the exception of occasional episodes of discomfort in the region of the right kidney which occurred at night, waking the patient from sound sleep. This discomfort was always associated with a distended bladder and was always promptly relieved upon voiding. A cystogram

made in March 1949, showed very definite reflux of urine at the right ureter (fig. 4, *B*). Immediately upon voiding a film in the upright position showed complete and rapid evacuation of the medium from the ureter, kidney pelvis and bladder (fig. 4, *C*). On May 25, 1948, the functional estimations from both kidneys showed an appearance time of 5 minutes with a 10 per cent concentration of dye in 15 minutes from the right kidney and from the left the appearance time was 4 minutes with 15 per cent excretion of phthalein in 10 minutes. No infection of any consequence has been present at any time during the patient's

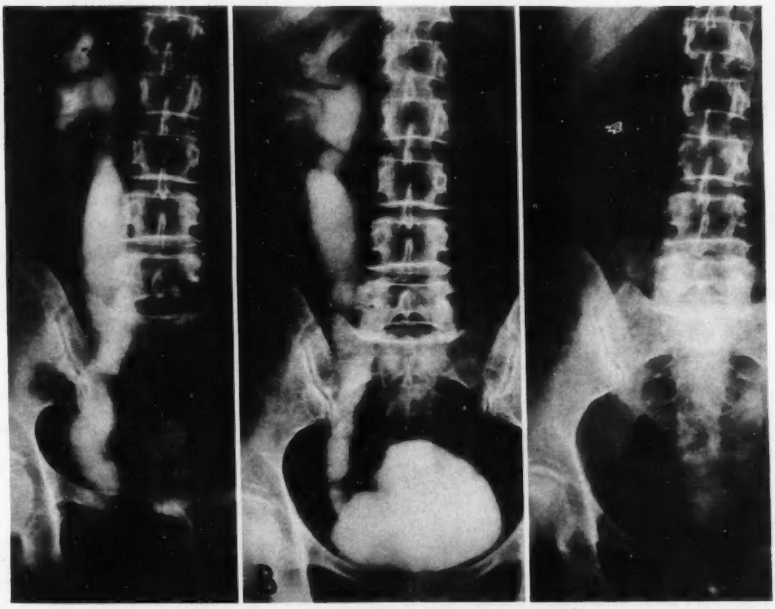

FIG. 4. *A*, right pyelo-ureterogram (vertical), showing retention due to ureterovesical obstruction. *B*, postoperative cystogram (horizontal), showing reflux due to enlargement of ureteral orifice. *C*, roentgenogram made immediately after voiding revealing complete emptying.

postoperative course. Insofar as can be determined, there has been no change in the size of the ureter or kidney pelvis since the surgery.

Case 2. B. H. K., a 14 year old white boy, was seen on June 3, 1946, with a history of recurrent attacks of pyuria, chills and fever since the age of 20 months. He had been seen by many physicians in different parts of the country, but had had no cysoscopic investigation as to the cause of the pyuria. The last severe attack was 3 months ago and consisted of severe hyperpyrexia and chills with marked frequency and burning on urination.

Physical examination revealed a very well developed and well nourished youngster who appeared to be in excellent health. Urinalysis showed numerous white blood cells and an occasional red blood cell, albumin 1 plus and specific

gravity 1.007. Culture revealed Staphylococcus aureus and Staphylococcus albus. The nonprotein nitrogen was 57 mg. per cent, in creatinine 2.8, white blood cells 12,700, red blood cells 4,625,000, hemoglobin 94 per cent; voided phenolsulfonphthalein was 85 per cent in 1 hour and 40 minutes.

Cystoscopy revealed marked gross trabeculation of the bladder walls, grade 3 to 4, with a bladder capacity of better than 700 cc. The ureteral orifices appeared fairly normal; there was no evidence of obstruction at the vesical outlet and no obstruction was noted in the posterior urethra. Catheterization of the right ureter with a No. 7 catheter revealed the presence of about 75 cc of residual

FIG. 5. Right pyeloureterogram (1946), showing dilatation. Left (not shown) showed same degree of dilatation.

urine, but no obstruction was apparent in the lower end of the ureter. The left ureter was found to contain 40 cc of residual urine. Intravenous phenolsulfonphthalein appeared from the right in 6 minutes with a concentration of 5 per cent in 15 minutes. On the left, the dye appeared in 4 minutes with a 10 per cent concentration in 15 minutes. Pyelograms revealed a marked dilatation of the right ureter with moderate pyelectasis with less marked dilatation on the left (fig. 5). Intravenous urograms disclosed very indistinct evidence of marked hydro-ureter and hydronephrosis on both sides.

The patient was admitted to the hospital on October 27, 1946, and on October 28, 1946, was taken to the operating room and a bilateral ureterovesical plastic procedure was carried out. The bladder was exposed by the utilization of a

transverse suprapubic approach. The peritoneum was reflected anteriorly from the entire dome of the bladder and from the lateral walls of the bladder down to and beyond the ureterovesical junction, exposing both of the iliac fossa. The surface of the bladder was found to be covered by enormous, tortuous dilated veins which were ligated with chromic catgut before opening the bladder transversely. The musculature of the bladder was found to be from 1 to 1.5 cm. in thickness. The transverse bladder incision was carried down to within 3 cm. of each ureteral orifice. A 20 curved metal sound was introduced through each orifice and the tip of the sound could be palpated within the ureter, which proved to be about 5 cm. in width just before entering the bladder.

By manipulating the sound and passing it downward, the tip could be felt some distance beneath the trigone, showing that the ureteral orifices were situated some distance above the sacculated ends of the ureters. It was quite obvious that the ureteral orifices needed to be enlarged downward through the trigone, as well as upward, in order to better guarantee drainage of the ureters. An incision measuring approximately 1 cm. in length was therefore made through both angles of the ureteral orifices which penetrated the vesical wall into the ureter. Atraumatic chromic catgut sutures were utilized to anastomose the mucosa of the ureter to the mucosa of the bladder. Care was taken not to penetrate through the bladder wall at any place and this was easily guarded against by keeping the lower end of the ureter in view at all times.

Despite the fact that the bladder was greatly enlarged in size, and the muscle walls quite thick, no evidence of vesical neck obstruction was observed. A 24 F urethral catheter was passed up each ureter with ease and left in place. A cigarette drain was placed in each iliac fossa and a suprapubic tube put in place. Closure was accomplished in the routine manner.

The patient's immediate postoperative course was uneventful and the temperature did not rise above 101.2F until the eighth postoperative day, when it rose to 105F, with pulse 120. Blood urea nitrogen 25 per cent, nonprotein nitrogen 48 per cent, white blood cells, 15,600. This was associated with extreme nausea and vomiting. Examination failed to reveal any costovertebral angle tenderness, but the patient was placed upon streptomycin without awaiting the report of cultures of his urine. After 24 hours his temperature returned to normal. An urinalysis at this time revealed many white blood cells with clumping and a trace of albumin. Culture of the urine revealed the presence of Proteus vulgaris and Aerobacter aerogenes. On the twenty-first postoperative day both ureteral catheters were removed together with the suprapubic tube. This was replaced with a 24 Foley catheter through the suprapubic wound. On the twenty-sixth postoperative day the suprapubic catheter was removed and the patient began to void 3 days thereafter. He was discharged from the hospital 45 days postoperatively feeling quite well with a blood urea nitrogen of 18.5 mg. per cent. The urine at this time contained a moderate number of white blood cells and the residual bladder urine was 150 cc.

Since operation the patient has had numerous cystograms (fig. 6, *A*) with the resulting finding of prompt reflux of the vesical contents up the ureters. In the

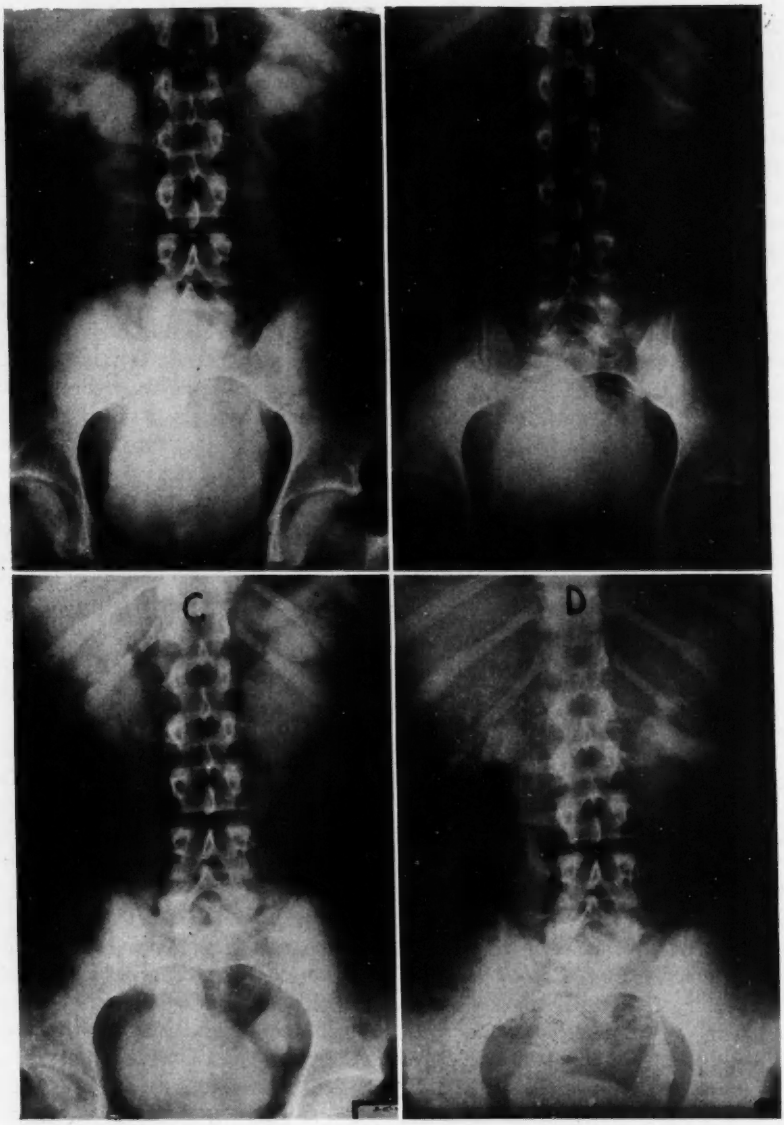

FIG. 6. *A*, cystogram (1947), showing reflux up ureters. *B*, cystogram (1949), made with patient in vertical position. Note absence of reflux in this position. *C*, urogram (vertical), during act of voiding showing reflux up ureters. *D*, urogram (vertical) at conclusion of urination showing small residuum.

upright position, during the act of voiding, the amount of dye in the ureters is perceptibly increased with associated increase in density (fig. 6, *B* and *C*). After voiding the ureters empty promptly into the bladder (fig. 6, *D*). There is no decrease in the size of the ureters. The patient has been completely free of any episodes of chills and fever and has enjoyed excellent health with normal growth development. At the present time he is piloting high speed motor boats as a recreation with no ill effects. Although the urine has remained infected, there have been no ill effects whatever from the pyuria. Estimations of his renal function by both blood urea nitrogen determinations, nonprotein nitrogen and creatinine have been slightly above the range of normal. In April 1949, the urea clearance test was 76 per cent and the voided phenolsulfonphthalein was 10 per cent in 30 minutes, 15 per cent in 60 minutes, 25 per cent in 90 minutes, giving a total of 50 per cent in 1½ hours. A cystometrogram made in April 1949 revealed a large atonic bladder of myogenic type with residual of 275 cc.

CONCLUSION

The surgical correction of ureterovesical obstruction is the production of vesicorenal reflux as a consequence. While this condition is unphysiological, it has been shown in the above case histories that the reflux is not incompatible, subjectively and objectively, with apparent good health and that the benefits derived from the relief of the obstruction may no doubt possibly outweigh the potential damage wrought by the reflux.

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DISCUSSION

DR. GEORGE SMITH (Brookline, Mass.): May I ask Dr. Emmett to say a word about his technique of resection, whether he cuts all the way around, resects until he sees the sphincter muscle, or how he does it?

DR. DAVID M. DAVIS (Philadelphia,Pa.): I am indebted to Dr. Emmett for having heard his excellent paper concerning the subject of transurethral resection of the vesical neck in adult women. A few of our fellow urologists have interested themselves in this subject and I think they have opened up a field which has been very widely neglected.

We have been interested in this subject for a long time, and it seems to us that in very many of these cases, the underlying difficulty is a congenital stenosis of the vesical orifice. The absence of marked pathological changes in the tissues shown in Dr. Emmett's slides would, I think, be corroborative evidence of this. Other corroborative evidence is the fact that such obstructions have been found in small children.

We have performed resection, or rather, punch operation, in little girls, of which the youngest was 4 years of age. Another was 6 years of age, and another one was 14 years of age. This case was of particular interest. Examination elsewhere had shown that one kidney was congenitally absent. The other kidney pelvis and the ureter were markedly dilated and there was a severe and chronic urinary tract infection, which made the little girl a semi-invalid, who had not responded to treatment consisting of frequent urethral catheterizations, pelvic lavage, and so forth.

Now, in this child, one could not say that there was real vesical trabeculation. One could outline the muscle bundles but little more. Neither was there any residual urine. The vesical orifice, however, was very small, and it was difficult for the child to urinate. She had to reinforce with her abdominal muscles.

We, therefore, performed a punch operation, removing several pieces from the vesical orifice. Since that day, the child has been perfectly well, the urine became sterile spontaneously and has remained so, the size of the ureter and pelvis has greatly diminished, the renal function is normal, and she has grown normally.

In another girl of 16, there had been severe urinary trouble all of her life, resulting in a loss of one kidney by nephrectomy for pyelonephrosis. In this case, the urethral obstruction was not due to a contracture or stenosis of the vesical orifice, but to a congenital valve lying about half-way along the urethra. Removal of this valve with a punch instrument produced a most dramatic and immediate cure of the patient, and she was able to void 400 cc at a time with perfect ease, and here again, the heavily infected urine became sterile spontaneously without any drug treatment.

Certainly, I think that most of us who go into this matter carefully would find that we cannot rely seriously upon either trabeculation or residual urine as a diagnostic index. The bladder oftentimes is able to compensate for obstruction

at the expense of increased intravesical pressure, which may indeed interfere, as it did in the 14-year-old girl, with the integrity of the upper urinary tract.

We have, however, at our command means which are perhaps better, certainly more objective. We can make graphic records by using the little machine called a Uroflometer, which has been described in the *Journal of Urology* by Dr. Willard Drake. This gives us the rate of flow of the urinary stream in cubic centimeters per second, and certainly if we find a markedly decreased flow rate through the urethra, associated with a normal or hyper-normal intravesical pressure as shown by cystometry, there must be obstruction; there cannot be anything else. We must therefore seek it, and we must find it. It is often, as Dr. Emmett has brought out, very difficult to see; very difficult indeed. But its relief, as he again has brought out, is usually followed by a most dramatic improvement or cure of the patient.

Dr. Fletcher H. Colby (Boston, Mass.): I wish very much to have some discussion of Dr. Orr's paper. The problem of dilated ureters in the young and in older people has been a very difficult problem with us.

We see a certain number of children at the hospital on the children's service, who have varying degrees of dilatation of their ureters. Some patients, however, are considerably older. I am frank to say that I know of no successful surgical operation that will take care of this situation We have tried most of the surgical procedures that have been advised.

Transplantation of the ureters to another part of the bladder has met with dire results in enough of these children so that I do not believe that that is the answer to the problem. We have had two recent instances where one ureter has been considerably dilated in older people, women around 35 or 45 years of age, and although the procedure we did on the people made no sense whatsoever, the results, at least the short-time results, were surprisingly good.

What was done there was to expose the lower ureter and remove by longitudinal section, a large portion of the ureter and sew it back together. I do not believe that this is the answer to the problem, either. I would like to hear a little more discussion from others who have had experience with this disease.

Dr. Herman L. Kretschmer (Chicago, Ill.): I wish to agree with Dr. Emmett in reference to his remarks about the difficulty in diagnosing these obstructions at the neck of the bladder, and also how little one sometimes sees on cystoscopic examination. His experiences dovetails with my experience and with that of Dr. Orr.

The presence of a thickened bladder wall with normal appearing ureteral orifices, and the presence of dilatation of the ureters with hydronephrosis should at once call our attention to the possibility of obstruction at or in front of the bladder neck.

Cause and effect I think were very obvious in one of Dr. Orr's illustrations in which he showed a progressive increase in the size of the bladder. This it seems to me was due to the unrelieved obstruction at the bladder neck.

The only other lesion that could result in this picture would be a lesion of the central nervous system.

Dr. Hibbs and I presented before this association a paper bearing directly on this subject. This was about 10 years ago.

It is my opinion that the procedure of making the ureteral orifice incompetent so as to increase ureteral drainage is of little if any value, since it does not remove the underlying cause. It was recommended by von Lichtenberg some years ago. It was without value in one case in which I used it.

Dr. George R. Livermore (Memphis, Tenn.): Dr. Emmett, I have had excellent results in cases of incontinence without a cystocele by applying the high frequency current in the internal meatus at 12, 3, 6 and 9 o'clock. The incontinence is frequently completely relieved and the residual greatly reduced in amount. Have you had a similar experience?

Dr. Edward W. Campbell (Philadelphia, Pa.): The operative procedure which Dr. Orr has presented suggests a rational approach to the solution of the problem of congenital hydro-ureter. In a discussion of the etiology and pathology of this congenital abnormality before this society last year, I attempted to demonstrate the sacculation of the juxtavesical ureter below the level of its intramural insertion. This sacculation, having been present in 4 of the 5 cases presented, suggested the necessity for the type of operative procedure Dr. Orr has demonstrated, in that it permits complete drainage of the ureter without obstruction.

Dr. Orr's procedure also suggests the possibility of a more uniform effective end result because the continuity of the ureteral wall is maintained in contrast to ureteral transplantation. The latter procedure has not been successful in our hands because of the large size of the ureter, and mainly, because of the atonicity of the ureteral wall.

Drs. Kretschmer and M. Campbell have stressed vesical neck obstruction as the etiologic factor. Our study suggested two separate pathological conditions only one of which can be caused by vesical neck obstruction. These were termed megalo-ureter, in which the ureteral orifice is atonic and congenital hydronephrosis, in which the ureteral orifice is normal and does not permit regurgitation on cystography. The proof for his contention was the unilateral occurrence of congenital hydronephrosis as demonstrated in 3 of the 5 cases presented.

Congenital hydronephrosis will require a procedure such as Dr. Orr has described for its correction. If, however, vesical outlet obstruction is present in conjunction with this hydronephrotic state, as is undoubtedly the case in Dr. Orr's patient, the creation of an incompetent ureteral orifice may hazard a successful end result.

Dr. Creevy: May I ask a question? Mr. Millin recently made the statement in a paper that ureterectomy done before the age of 5 years in congenital dilatation of the ureters is curative. Can anybody substantiate or refute that statement?

Dr. George G. Smith (Brookline, Mass.): I was very much interested, particularly in the papers of Dr. Emmett and Dr. Orr, because I have had experiences, both good and bad, in both lines.

I was not going to discuss Dr. Orr's paper because I did not bring with me some

slides which would be really necessary to make a complete discussion, but Dr. Colby has said that there was no record of any successful case done by transplantation of the ureter at the General.

DR. COLBY: No, that is not so. I said that my experience with it had not been good.

DR. SMITH: Oh, I beg your pardon! At any rate—I misunderstood you—there was one case which I did when I was on the service, of a little girl with unilateral dilatation of the ureter, very marked. She had attacks of fever and chills, constant urinary infection, and in trying to decide what to do about her and in looking up some of the literature, I found Frank Hinman's paper of 1928, in which he treated that subject; it seems to me that his remarks were very important.

He pointed out that the sharp angulations in the over-dilated ureter were the cause of retention, to a considerable degree. He advocated nephrostomy first, and then resection of the redundant ureter after it had been freed so the kinks were straightened out.

With this little girl, who was, I think, 3 or 4 years old, I did not do a preliminary nephrostomy, but I operated suprapubically. She had no residual urine, but I don't remember whether her bladder was thickened. The lower ureter was freed from the bladder, the redundant ureter was drawn down, and 4 or 5 cm. of ureter were cut off. The ureter was then implanted in the bladder by practically a Coffey I technique. The last x-ray which I have of that child was some 2 years later, at which time her ureter looked straight and was not dilated anything to speak of.

She was recently seen, some 5 years after operation, in the out-patient clinic of the General by the Children's Department and the doctor who saw her there told me that she was in good condition and had no more attacks of chills and fever.

There was another patient I did who did not do so well, but I do think that is a possible way of handling these cases, and it seems to me one that should be seriously considered.

DR. MEREDITH F. CAMPBELL (New York, N. Y.): I am greatly interested in Dr. Emmett's presentation from the standpoint of etiology in these cases. He did not have time to go into the past history of these women, but from my experience, I strongly suspect that much of the obstructive pathology had its origin on a congenital basis or in early childhood. The reason for feeling so is that on examination of a fairly large series of enuretic children (we have now examined over 1500) who had functional enuresis presumably, and who had been subjected to at least three to four months of intensive medical and psychotherapeutic endeavor, we found a little over 12 per cent had residual urine. Yet they still manifested their so-called enuresis.

I disagree with the speaker who a little while ago said that residual urine was of no consideration. To me, it is an indication of bladder wall decompensation, whether it is of dynamic or adynamic origin. In the series of cases of enuretic children just referred to, a great many had true obstructive lesions that you could

put your finger on, as it were. A great many simply showed congenital narrowing in the lower urethra. Many of them had stricture of the external meatus. Others had narrowing of the vesical oulet, and in many of these the obstruction was relieved by transurethral resection. A gratifying number responded well to simple instrumental dilatation of the urethra.

I have had no opportunity to observe most of these children as they progressed to later life; in Dr. Emmett's cases, it is entirely possible that the pathological sequence which ultimately terminated in acute retention often began early and on a congenital basis.

Dr. Kretschmer pointed out many things that I also had in mind but chiefly the possible multiplicity of congenital obstructions or congenital lesions elsewhere. I am sure you all have seen in the same patient, usually a child, contracture of the bladder neck, pin-point ureteral orifices, and some with ureteropelvic obstructions as well. In short, the identification of the ureterovesical junction stricture or the controlled bladder outlet is not enough. The transplantation of the ureter (ureteroneocystostomy) for ureterovesical junction stricture in these young children seems needlessly traumatic. I have done it in some children but the results have not been satisfactory in my hands. The procedure that Dr. Orr indicated has been the best method of surgically treating ureterovesical junction strictures that I have encountered. At operation, you will often find that the ureteral opening is extremely small, and in carrying out the procedure, I like to use a small curved bistoury, the Weber iridectomy knife. It has a small ball point on the tip which can be introduced into an extremely small meatus into which one may be unable to pass a grooved director or a small sound upon which to cut down.

In making this incision up the ureter to divide the stricture, one should cut widely. We frequently carry the incision well ouside the bladder, intubate the ureter adequately (14–20 F), leave the bladder wide open and through this opening bring out the ureteral tube or tubes as well as a suprapubic tube. I have a 6-months-old boy in the hospital now on whom I operated about a week ago for the same condition. A No. 20 catheter was left indwelling in each ureter and kept there for 10 days or so. It is unnecessary to suture the incised ureteral mucosa to the vesical mucosa, although if it can readily be done, healing may be expedited.

I am sorry I do not have for Dr. Orr the follow-up films on his patient whom he was good enough to let me see, but our office records show that I gave them to the parents when they left town. In this case, the progressive dilatation of the bladder strongly suggests that the boy has an intravesical obstruction which may very well need surgical relief.

After these various plastic procedures have been satisfactorily carried out, the anatomic changes due to back-pressure damage and infection are largely permanent. We strive chiefly for physiologic restitution. It is my experience that these children usually maintain their large ureters yet the renal function improves as does weight, general condition, and gastro-intestinal function. Still,

the child has been helped even though the ureters stay as large as the small bowel.

Dr. David M. Davis (Philadelphia, Pa.): May I make a corrtion? I am afraid that I did not make myself clear to Dr. Campbell and perhaps to others. I had no intention of saying that residual urine is of no importance. Perhaps it would make it clearer to say that it is my opinion that the absence of residual urine does not rule out vesical neck or urethral obstruction.

Dr. John L. Emmett (Closing discussion): Dr. Smith has asked me to discuss briefly the technique of transurethral resection in women. We employ the cold knife punch. In all cases tissue is removed from the entire circumference of the vesical neck and proximal third of the urethra. In an occasional case the resection has included the proximal half of the urethra. A good rule of thumb, however, is that if the resection is confined to the proximal third the patient's continence will not be compromised. There is a little trick that may be helpful. After resection is begun it is often difficult to judge one's position in the urethra. To avoid this it is best not to remove tissue from the 6 o'clock position until the resection is almost completed. The normal appearing uncut vesical neck in this area may then be used as a landmark much as one makes use of the verumontanum of the male during transurethral prostatic resection.

The question has been asked as to how deeply one cuts during resection. This is a little difficult to answer as it is learned only by experience. In a large percentage of cases the resection has to be done in two stages because enough tissue has not been removed at the first sitting. It is surprising the quantity of tissue that can be removed in some cases. As a general rule, one can cut more deeply than is anticipated. It is well to remember that at the second sitting tissue can be removed more easily and safely than at the first operation. One must be careful of the posterior vesical lip, especially in children, as it is fairly easy to cut or fulgurate too deeply and produce a vesicovaginal fistula. Experience has shown that when substantial amounts of tissue are removed, the bulk of the tissue is removed from the anterior three-fourths of the quadrant.

Dr. Jewett asked about the incidence of incontinence following transurethral resection in women. It has been very low. I did not have time to mention it in my presentation today but it is presented in detail in the paper as it will be published.

Dr. Meredith Campbell's comments concerning the possibility of subclinical congenital obstruction of the vesical neck in female infants being one of the underlying etiological factors in vesical retention in later adult life is most interesting and plausible. We recognize this clinical entity in males, and there is no reason why it should not be a factor of importance in females.

Dr. Louis M. Orr (Closing discussion): I think that perhaps I made an error in trying to say too much in too few minutes and did not make myself clear on certain things with regard to these obstructions.

I agree perfectly with Dr. Kretschmer. I mentioned a little while ago that this boy unquestionably had some obstruction of the bladder neck. I cannot

conceive of all that damage over all these years without something going on at the vesical outlet, but at the same time I also mentioned the fact that these parents do not wish anything done if they can possibly avoid it, until this youngster is married, for the sake of carrying on the family name. Once we go in with a cystoscope, we know very well that the ejaculate will be deposited down in the bladder and not out in the urethra.

In relation to Dr. E. W. Campbell's suggestion, I think, again, I was in error in not explaining those slides. I would like to have slide No. 3, if I could. I understand that the operator has gone. Well, those slides did show that the incision was extended downward as well as upward, and in the fourth slide, you noticed that the sacculation had been corrected by this large orifice. But I think it most important that this incision be carried down to where the entire ureter can be drained, if possible.

Now, as to this boy with these enormous ureters, I wouldn't dare risk the possibility of damage by trying to reimplant such ureters into the bladder, and I don't think anyone else would. These are the type of cases you see where something has to be done to relieve the retention, and I don't know of anything else except to produce a reflux and let him go ahead and live out his life span, whatever that might be. As Meredith Campbell said in a letter to me: "Although prognosis is grave, he may live to bury us all"; and at the present moment he is doing beautifully. His urea clearance is now about 76 per cent; the phenolsulfonphthalein excretion, 90 minutes; after voiding and catheterization, 55 per cent, which is very good. The blood urea is 18, and his other blood studies run along in a sort of normal fashion and he is not annoyed by the pyuria. He does not get up at night. I think at some time we must do something about that bladder obstruction, unquestionably.

Dr. Creevy raised the question about presacral neurectomy done before the age of 5 years. I should think in these conditions which probably begin in embryo or at least in fetal life, the cement has been pretty well set in the ureteral walls, and I can't imagine that they would retract down to where they would become normal ureters, because undoubtedly there is a considerable amount of muscular hypertrophy in the walls before they will begin to fade away into thinness, which is commonly seen.

I was glad to hear of Dr. Smith's successful reimplantations, but the incidence of failure reported in the literature is extremely high. Dr. Jewett just mentioned to me that Dr. Parke Smith has several patients who have had beautiful results from reimplantations. The ureter in the adult female might have been reimplanted with good results, but even there you run the risk of losing the kidney on whichever side you operate.